MAN-MADE VITREOUS FIBERS

Published By

NAVY ENVIRONMENTAL HEALTH CENTER
2510 WALMER AVENUE
NORFOLK, VIRGINIA 23513-2617

OCTOBER 1997

Reviewed and Approved by

CAPTAIN R. L. BUCK, MC, USN
Commanding Officer

TABLE OF CONTENTS

ABBREVIATIONS

EC - degrees Centigrade

EF - degrees Fahrenheit

Fm - micrometer; 10^{-6} meters

f/cc - fibers per cubic centimeter of air

f/cm^2 - fibers per square centimeter

f/ml - fibers per milliliter; equivalent to f/cc (1 ml = 1.000027 cc)

g/cc - grams per cubic centimeter

mg/m^3 - milligrams per cubic meter of air

ACGIH - American Conference of Governmental Industrial Hygienists

AM - alveolar macrophage

CAS - Chemical Abstract Service number; a unique identifier code assigned to a material

CHL - Chinese hamster lung

CHO - Chinese hamster ovary

ECFIA - European Ceramic Fiber Industry Association; a trade association of RCF manufacturers in Europe

EPA - Environmental Protection Agency

GA - general area

HD_{50} - hemolytic dose 50; the dose needed to cause hemolysis in 50% of the cells tested

HEPA - high efficiency particulate air; a type of filter defined by its ability to capture 99.97% of 0.3Fm diameter mon-dispersed particles.

IARC - International Agency for Research on Cancer; an agency of the World Health Organization that evaluates the carcinogenic risk of materials for humans.

IH - industrial hygienist or industrial hygiene

IRIS - Integrated Risk Information System; produced by EPA

JM - Johns Manville, a manufacturer of MMVF products, particularly glass.

LDH - leucine dehydrogenase

LM - light microscopy

LPM or lpm - liters per minute

MMMF - man-made mineral fiber(s)

MMVF - man-made vitreous fiber(s)

mppcf - millions of particles per cubic foot of air; mppcf x 35.3 = million particles per cubic meter = particles per cubic centimeter

MSDS - material safety data sheet

NAVOSH - Navy Occupational Safety and Health

NIOSH - National Institute for Occupational Safety and Health

NMRD - non-malignant respiratory disease

NTP - National Toxicology Program

OR - odds ratio; the outcome measure of statistical association in a case-control study, which estimates the relative risk under a specific set of conditions (control groups).

OSHA - Occupational Safety and Health Administration; agency of the U.S. Department of Labor, charged with developing and enforcing occupational standards (regulations)

P & CAM - analytical method for fiber counting

PAH - polycyclic aromatic hydrocarbons

PCM - phase contrast microscopy; analytical method used for fiber counting

PCOM - phase contrast optical microscopy; same as PCM

PEL - permissible exposure limits; legal values, published by the Occupational Safety and Health Administration.

PLM - polarized light microscopy; analytical method used for fiber identification according to refractive properties of the crystalline structure.

RCF - refractory ceramic fibers; a type of MMVF used in extremely high heat applications, such as kiln and furnace linings.

RCFC - Refractory Ceramic Fiber Coalition; an association of RCF manufacturers who develop and promote safe practices for RCF, support and conduct RCF research and practice product stewardship.

REL - recommended exposure limit

ROM - reactive oxygen metabolite

RTECS - Registry of Toxic Effects of Chemical Substances

SCE - sister chromatid exchange

SEM - scanning electron microscopy

SMR - standardized mortality ratio; a ratio of observed deaths in a disease study group (cohort) to the number that would be expected if the cohort were subjected to the risks (rates) from an appropriately matched standard population

SNUR - significant new use rule; published in 40 CFR, Subchapter R (Toxic Substances Control Act), Part 721, Significant New Uses of Chemical Substances

SVF - synthetic vitreous fibers

TD_{50} - toxic dose 50: the dose needed to cause a toxic response in 50% of the cells or animals tested

TEM - transmission electron microscopy; used to count and identify fibers through chemical composition

TIMA - Thermal Insulation Manufacturers Association; trade association of MMVF manufacturers

TLV® - Threshold Limit Values®, published by the American Conference of Governmental Industrial Hygienists

TWA - time weighted average; the concentration of a contaminant that has been weighted for the time duration of the sample

WEL - workplace exposure limit

INTRODUCTION

Man-made vitreous fibers (MMVF), also called man-made mineral fibers (MMMF) and synthetic vitreous fibers (SVF), are a group of fibrous, inorganic materials, generally aluminum or calcium silicates, that are derived from rock, clay, slag and glass. These materials are widely used for thermal and acoustical insulation, plastics reinforcement and textile manufacturing. There are three categories of MMVF: (1) glass fibers, both glass wool and continuous filament (textile) glass; (2) rock wool and slag wool, often referred to collectively as mineral wools; and (3) ceramic fibers, both textile and refractory.

The commercial production of MMVF became especially important when the adverse health effects associated with asbestos prompted the search for a substitute material. Despite some chemical and morphological similarities between asbestos fibers and MMVF, the scientific community initially agreed that the vitreous fibers were innocuous. However, in 1972, Stanton and Wrench reported that glass fibers implanted in the pleural cavity of rats produced mesothelioma. Although the exposure route in the study circumvented normal inhalation defense responses, the report initiated the intensive research that continues today.

Since the early 1970s, the experimental evidence on MMVF has sparked controversy in the scientific community. There is little agreement on the human health impact, particularly for long term inhalation. Some early animal toxicity data showed an association between the fibers and disease induction, but the exposure routes were mainly artificial, such as injection or implantation. Consequently, the last five years or so have been devoted to intensive animal inhalation studies. With a few exceptions, these results do not support the carcinogenicity of the fibers, but do indicate that they are fibrogenic. Early epidemiological evidence indicated a positive correlation between human disease and MMVF exposures, but follow-up surveys correcting for other exposure sources are finding that the correlations are less certain.

Extensive use of these materials in both occupational and non-occupational settings requires that occupational health professionals stay informed on the current toxicological and epidemiological evidence. This document consolidates and presents such information in an effort to assist industrial hygienists, occupational medicine physicians, and other Navy medical department professionals in making informed decisions about the health hazards associated with these fibers. Topics include exposure issues, air sampling information, personal protective equipment and regulatory standards. The manual also reviews fiber morphology and deposition, since the nature of the fiber and its respirability govern its hazard potential.

This manual updates the October 1990 publication of the same title (NEHC-TM91-1). For the most part, information in the original publication is retained in this manual. Because much new information has been incorporated throughout, you will get the most benefit by reading this manual in its entirety.

Questions and comments are welcomed, and may be directed to our Industrial Hygiene Directorate at (757) 363-5522, DSN 864-5522, or email plkrevonick@nehc.med.navy.mil.

PRODUCTION AND USE

Production

Though MMVF manufacturing processes vary with the fiber being produced and its intended application, all fiber production involves three general processes. The raw materials are first put in a furnace or cupola to liquefy and form a homogeneous melt. The liquid can then be removed to solidify into a preform (e.g., marbles) for future remelt or can be used immediately in a fiber production process. Once the fibers are made, the final step forms or packages the fibers into the desired commercial product.

The actual fiber forming process is specific to the end product, but again some generalities apply. Continuous fibers or filaments are made by drawing or spinning, a method that extrudes the molten mix from nozzles or through a series of rapidly rotating wheels. These fibers are used mostly for textile applications (TIMA, 1990).

Insulation wools are usually manufactured with the rotary or centrifugal process. The molten material falls into a rotating spinner, and fiber attenuation occurs as centrifugal force extrudes the material through holes in the spinner sidewalls. The term "wool" is used to describe these fibers because they are made without using a nozzle. The final fibers are generally longer and finer than those produced by drawing, though fiber diameters tend to be more variable.

Flame attenuation, used to make extremely thin special purpose fibers, is a two step process. An initial coarse fiber filament is produced by drawing. These primary fibers are remelted in a jet flame blast to further attenuate the fiber (TIMA, 1990).

Following fiber formation or during fiber conversion to the commercial product, fiber utility can be enhanced by adding binders, sizings, and/or lubricants. Bindings are usually phenol-formaldehyde resin mixtures that give structural rigidity to the fiber. Off-gassing studies conducted by the Thermal Insulation Manufacturer's Association have shown that the cured end products do not generate any appreciable amounts of the chemicals (TIMA, 1990).

Lubricating oils, paraffin oils, or other specially formulated oils may be atomized over the fibers to reduce dust and lint generation of the bulk product (IARC, 1988; TIMA, 1990). Cherrie and Dodgson (1986) estimate that this application can decrease the generation of airborne fibers during use by a factor of ten.

If the end product will be used for reinforcement applications, sizings are added to promote adhesion between the fibers and the matrix material (Mettes, 1975). There are a variety of sizings used, including polyvinyl acetate chrome chloride mixture, polyvinyl acetate silane, polyester silane, and epoxy silane (TIMA, 1990). Depending on additional processing steps required, sizing chemicals may be retained, altered or even removed from the end product fibers.

This is a simplified overview of how vitreous fibers are made. Their actual composition and the characteristics that make each type of fiber unique warrants individual attention. This will be discussed in the section on physical and chemical characteristics.

Uses

The majority of MMVF products are used for thermal and acoustical insulation. The loose wools provide home attic and interjoint insulation. Bulk fiber products can be incorporated into ceiling tiles for both fire resistance and sound insulation. MMVF are also made into blankets, batts, boards, and pipe sleeves (NIOSH, 1977a, 1980). Refractory ceramic fibers are also used for insulation, but in applications requiring extreme temperature resistance. Some examples include furnace and kiln linings, heat/fire containment walls and catalytic converter blankets in aircraft engines.

Glass fibers are often used in thermoplastics reinforcement, especially for aircraft and marine hulls, though these applications are more in the advance composite material arena (TIMA, 1990). A more common reinforcement use for MMVF is in paper, tape, high temperature fabrics and cables (NIOSH, 1980; TIMA, 1990).

Special purpose fibers, particularly glass, may be used for air and liquid filters. The aerospace industry uses vitreous fibers for high temperature resistance applications such as motor shrouds (IARC, 1988). Today's fiber optics for communication, light, and image transmission are possible because of continuous filament glass fibers.

A relatively recent use for rock and slag wools has been found in the horticultural arena. The wools are being successfully used in Europe as a bedding medium for seedlings (TIMA, 1990).

CHEMICAL AND PHYSICAL PROPERTIES

Though commonly used, the term man-made mineral fibers (MMMF) does not correctly describe the nature of the fibers. By definition, a mineral is naturally occurring and usually crystalline, yet the fibers we review in this document are synthetic and amorphous. Man-made vitreous fibers (MMVF) or synthetic vitreous fibers (SVF) are more correct terms for the fiber family and are preferred.

Asbestos and other naturally occurring mineral fibers are characterized by their crystalline structure and chemical composition. In contrast, the man-made vitreous fibers are amorphous; that is, they are glassy, with no discernible crystalline array when examined by x-ray diffraction. Their chemical composition is dependent on the original material used to manufacture the fiber. Since MMVF are not crystalline, they do not split longitudinally into thinner fibers like asbestos, but rather break transversely into shorter pieces.

MMVF do have some of the same morphological characteristics as the amphibole asbestos fibers. In fact, it was the suggestion that the shape and size of a fiber was related to its potential for carcinogenicity that prompted researchers to study the vitreous fibers (Stanton and Wrench, 1972).

Fibrous Glass

Fibrous glass products begin with finely powdered sand as the major silica source. Additional oxides, added in varying proportions, will dictate the final chemistry of the fiber. Typical ingredients include aluminum oxides from kaolin clay and from synthetic sources, calcium and magnesium oxides from dolomite and boric acid derived from a natural source of calcium borate (NIOSH, 1980; IARC, 1988; TIMA, 1990). Table 1 shows the composition of typical glass fibers.

Table 2 shows glass composition variations for the different types of glass used in commercial fiber manufacture. Though varied to meet the end use requirements of the fiber, the basic composition is constant. The chemical properties of the fiber are also dictated by the glass "recipe." For example, if the fiber has a low percentage of alkali metal oxides (K_2O, Na_2O_3, Li_2O) and a higher relative percentage of the alkali earth metals (Ca, Mg, Fe), it will have a lower chemical resistance. This particular type of fiber is manufactured as "water soluble glass" (TIMA, 1990).

The density of fibrous glass products is rather uniform - 2.568-2.605 grams per cubic centimeter (g/cc) for most, with high lead silicates averaging about 4.3 g/cc. Refractive indices vary from 1.512 to 1.549 (NIOSH, 1977a; TIMA, 1990).

Typical diameters of fibrous glass are shown in Table 3. Average lengths are greater than 250 micrometers (Fm).

Table 1. Typical glass fiber composition (adapted from NIOSH, 1977a)

Component	% by Weight	Component	% by Weight
SiO_2	34-73	K_2O	0-3.5
Al_2O_3	3-14.5	ZrO_2*	0-4
CaO	0-22	TiO_2*	0-8
MgO	0-5.5	PbO**	0-59
B_2O_3	0-8.5	F_2*	0-2
Na_2O_3	0.5-16		

* usually seen only in lime-free borosilicates

** seen only in high lead silicates

Table 2. Composition variance (% by weight) for different glass types (compiled from Mettes, 1975; NIOSH, 1977a; IARC, 1988)

	GLASS TYPE*			
Component†	E	C	S	AR
SiO_2	55.2	65	65	60.7
Al_2O_3	14.8	4	25	--
CaO	18.7	14	--	--
MgO	3.3	3	10	--
B_2O_3	7.3	5	--	--
Na_2O	0.3	8.5	--	--
K_2O	0.2	--	--	2
ZrO_2	--	--	--	21.5
Li_2O	--	--	--	1.3
F_2	0.3	--	--	--
Fe_2O_3	0.3	0.3	trace	trace

† Components may also include phosphorus, titanium, lead, copper, tin and beryllium oxides.

* Glass type:

E glass - electrical glass, so called because the low alkali oxide content makes it excellent for electrical applications. Over 99% of all continuous filament glass is this type. Insoluble in hydrochloric acid; specific gravity 2.54 g/cc; melting point 1555EF (846EC); refractive index 1.547.

C glass - chemical glass, named because it is chemically resistant to acids. Typically used for glass wool. Specific gravity 2.49 g/cc; melting point 1380EF (749EC).

S glass - high tensile strength glass, 33% greater strength than that of E glass. It is produced only in the United States for high technology uses. Specific gravity 2.49 g/cc; melting point 1778EF (970EC); refractive index 1.523.

AR glass - alkali resistant. Capable of reinforcing 20-30 times its weight. Often used for cement reinforcement. Differs from the other glasses by the presence of zirconium.

Table 3. Fibrous glass diameters, micrometers (adapted from NIOSH, 1977a; Head and Wagg, 1980; Lockey, 1981; TIMA, 1990)

Type of Fiber	Typical Diameter	Diameter Range
Continuous filament	6-15	3-25
Ordinary glass wool	3-7	3-15
Special purpose	1-3	0.1-10
Special purpose, fine	# 1	0.05-3

Christensen *et al*. (1993) measured fiber diameter distributions in 22 MMVF product samples from 11 manufacturers. Measurements were made with light microscopy (LM) and scanning electron microscopy (SEM). Included in the analysis were 9 glass wool samples with the following results: LM - arithmetic mean diameters 2.4-8.1 Fm and geometric means 1.7-6.6 Fm; SEM arithmetic means 1.2-7.7 Fm and geometric means 0.8-6.3 Fm. There was a single special purpose fiber product sample, with SEM arithmetic mean diameter 0.6Fm and geometric mean 0.4Fm (LM not recommended for fine fiber analysis due to lack of resolution).

Rock Wool and Slag Wool

The term "mineral wool" is often used to refer collectively to rock wool and slag wool, though glass wool is sometimes included in this term as well. Because the rock and slag wools have different origins and differ chemically, they should be identified individually whenever possible.

Like the other MMVF, rock and slag wools are predominantly calcium and aluminum silicates. As a group, however, these wools tend to be richer in the alkali earth metal oxides (i.e., Ca, Fe, Mg, Ti), and to have lesser amounts of the alkali metal oxides (i.e., K, Na) than do the other man-made fibers.

Rock wool begins with igneous rocks such as diabase, basalt or olivine. These natural rocks are 40-60% calcium and magnesium carbonate (NIOSH, 1980; TIMA, 1990). Rock wool will dissolve in hydrochloric acid.

Slag wool is produced by recycling certain blast furnace wastes. Naturally, the final product composition varies with the metallic content of the slag originally used. Slag wools typically lack significant amounts of sodium. They are usually slightly soluble in hydrochloric acid.

The chemical composition of typical rock and slag wools is in Table 4 (adapted from NIOSH, 1977a, 1980; TIMA, 1990):

Table 4. Typical rock and slag wool chemical compositions (in %)

Component	Slag Wool	Rock Wool
SiO_2	32-41	45-52
CaO	27-40	10-12
MgO	4-13	8-15
Al_2O_3	8-15	8-13.5
K_2O	0-0.5	0.8-2.0
Na_2O	0-2	0.8-3.3
TiO_2	0-0.5	1.5-2.7
Fe_2O_3	0-2	5.5-6.5
S	0-2	0-0.2
P_2O_5	0-1	--
MnO	0.1-0.5	0.1-0.3

The final chemical proportions of the wool products are controlled by balancing the acid to base ratio of the melt. The total percentage of silicon dioxide and aluminum oxide form the acid portion, whereas the base is the sum of calcium and magnesium oxides (TIMA, 1990). The acid-base ratio is important in determining the viscosity of the melt.

Rock wool and slag wool have melting temperatures of 2100EF (1149EC), thus making them excellent candidates for high temperature insulation applications. Table 5 summarizes the physical characteristics (adapted from TIMA, 1990). According to Cherrie *et al*. (1986), these wools have nominal diameters of 3-8 Fm.

Though not seen in modern rock and slag wool products, fibers made before the early 1970s were often contaminated with asbestos, especially if the fibers were used for cement reinforcement (Cherrie and Dodgson, 1986). In addition, copper slag was frequently used to make slag wools, thereby introducing arsenic into the manufacturing process.

The fiber dimension study by Christensen *et al*. (1993) included 9 rock and slag wool product samples. Using light microscopy, diameter arithmetic means ranged from 2.5-4.7 Fm, with geometric means of 1.7-3.3 Fm. With SEM analysis, arithmetic mean diameters were 2.4-5.3 Fm; geometric means were the same as LM - 1.7-3.3 Fm. These wools were also ignited to remove binder and shot. Although this shortened some fibers, the authors state that there was no effect on diameter.

Table 5. Mineral wool chemical characteristics

Property	Slag Wool	Rock Wool
Melting temperature, EF (EC)	2100-2300 (1149-1260)	2100-2300 (1149-1260)
Specific gravity, g/cc	2.7-2.9	2.7-2.9
Refractive index	1.6-1.8	1.6-1.8
Tensile strength, x 10^3 psi	70-100	70-100
Non-fibrous component, % (% shot)	30-50	20-50

Refractory Ceramic Fibers

Refractory ceramic fibers (RCF), though representing only 2% of the total MMVF production market are the most specialized of the fibers. Their primary use is in high temperature applications where resistance to about 3000EF (1649EC) is required. These fibers may also be called refractory fibers or ceramic fibers.

RCF can be loosely grouped into three categories based on the ingredients: (1) kaolin clay based; (2) aluminum silicate and metallic oxide blends (i.e., chromous or zirconia); and (3) high purity aluminum silicate. The fibers may contain trace amounts of other metal oxides, usually boron, titanium, magnesium and/or chromium, depending on the final product requirements. For especially high temperature applications, fibers are made with more than 90% zirconium oxide (TIMA, 1990). There are also non-oxide ceramic fibers - such as silicon carbide, silicon nitride and boron nitride - but these are crystalline forms and therefore not included in the MMVF family.

Refractory ceramic fibers are unique in that, although initially manufactured as amorphous fibers, they have been found to devitrify, or crystallize, when exposed to extreme heat. As the temperature reaches about 980-1000EC, the alumina-silica matrix (usually about a 50-50 mix) undergoes chemical changes to mullite, an aluminosilicate crystalline compound. When temperatures increase to 1050-1100EC, excess silica begins to crystallize to cristobalite (IARC, 1988; TIMA, 1990). This is extremely important from a health hazard standpoint, since cristobalite, as silica, is considered "carcinogenic to humans" (IARC, 1996). With

greater increases in temperature, the concentration of mullite stays about constant. Cristobalite conversion reaches its maximum at 1200EC, and by 1400EC, the cristobalite converts to a viscous liquid phase.

Fibers having a high percentage of aluminum oxide and zirconium oxide are able to retain their physical and chemical qualities even when subjected to extremely high temperatures. The fibers are resistant to oxidation, reduction and most corrosives. They will, however, succumb to attack by some acids (i.e., phosphoric) and concentrated alkalis (IARC, 1988; TIMA, 1990). Addition of zirconia and chromia oxides also stabilize the cristobalite phase such that it can undergo much higher temperatures before entering the liquid phase.

Three RCF product samples were evaluated for fiber diameters in the Christensen *et al.* (1993) study. Results were: LM arithmetic mean - 2.3-3.7 Fm, geometric mean 1.5-2.8 Fm; SEM arithmetic mean - 2.4-3.8 Fm, geometric mean range 1.7-2.8 Fm.

Tables 6 and 7 summarize some RCF properties.

Table 6. Fiber analysis, in percent by weight, of some commercial ceramic fibers (adapted from IARC, 1988)

Component	Fiberfrax® bulk	Saffril® (aluminum bulk)	Fireline ceramic
Al_2O_3	49.2	95.0	95 to 97
SiO_2	50.5	5.0	
ZrO_2	--	--	--
Fe_2O_3	0.06	--	0.5-1.0
TiO_2	0.02	--	0.7-1.3
K_2O	0.03	--	--
Na_2O	0.20	--	0.1-0.2
CaO	--	--	<0.1
MgO	--	--	trace
Y_2O_3	--	--	--
B_2O_3	--	--	<0.1

Table 7. Some physical properties of ceramic fibers (adapted from IARC, 1988; TIMA, 1990; Kojola and Moran, 1992)

Refractive index	1.55 - 1.57
Specific gravity, g/cc	2.6 - 3.0 alumina bulk = 0.096; zirconia bulk = 0.24 - 0.64
% Non-fiber (shot)	40-60% by weight
Softening point	1700 - 2000EC zirconia bulk = 2600EC
Mean diameter	2 - 6 Fm overall; 8 - 12 Fm for continuous filament; 1.2 - 3 Fm for blown/drawn fibers
Mean length	2 - 254 Fm

SAMPLING AND ANALYSIS

Sampling methods are dictated by the standard used. The Navy currently uses dust standards, so samples are collected and analyzed gravimetrically (i.e., as milligrams per cubic meter or mg/m^3). In 1996, the ACGIH proposed fiber TLVs® (f/cc) for synthetic vitreous fibers (SVF), with analysis done using the NIOSH fiber counting procedure. Except for refractory ceramic fibers (which remained on the Notice of Intended Changes), SVF TLVs® for were moved to the adopted values in 1997.

Gravimetric

Air samples for MMVF as dusts can be collected using methods 0500 and 0600 in the NIOSH manual of analytical methods (NIOSH, 1994). These are the sampling and analysis criteria for particulates not otherwise regulated, total and respirable, respectively. The individual methods list sampling protocol, measurement techniques, and method accuracy data. Since the respirable fraction is the one of interest, it is the collection procedure of choice.

The main objection to using gravimetric procedures is that all dust in the sample area is collected. Other than additional evaluation of the filter (i.e., by scanning or transmission electron microscopy, (SEM or TEM)), there is no way to identify whether the total weight of the dust is truly reflective of the particular fiber being sampled. As shown by Jacob *et al*. (1993) during studies at Owens-Corning Fiberglas® plants, typically less than half of the total airborne fibers were glass (actual percentages, based on reported fiber means, ranged from 26-70% glass). Though non-glass fibers were not identified, the authors noted that a significant number of them appeared to be cellulose fibers.

Fiber Counting

Airborne fiber samples can be collected and analyzed with method 7400 from the NIOSH manual of analytical methods (NIOSH, 1994). Samples are collected on 25 mm cellulose ester filters using a conductive cowl, the filter is cleared, and counting is done using phase contrast microscopy (PCM). There are two sets of counting rules: (1) the A rules stipulate that only fibers >5Fm long and with a length to width ratio $3:1 will be counted; (2) the B rules define a fiber as >5Fm long and <3 Fm in diameter, with an aspect ratio $5:1. The B rules also count fiber ends rather than individual fibers. NIOSH (1994) recommends using alternate counting rules for "...non-asbestos fiber types, such as fibrous glass." This includes the B rules, the WHO reference method (WHO, 1985) and the NIOSH fibrous glass criteria document method (NIOSH, 1977a).

TIMA (1990) suggests that the B rules will produce counts that more closely quantify the actual respirable exposures of MMVF. The upper diameter limit for respirable fibers is accepted as 3 Fm (Esmen *et al.*, 1978; WHO, 1985) or 3.5 Fm (NIOSH, 1977a; IARC, 1988). Except for the special purpose fibers, MMVF products generally contain a significant fraction of airborne fibers having diameters greater than

3-3.5 Fm . Consequently, the A rules will yield higher respirable fiber counts than those obtained with the B rules simply because non-respirable fibers will be included. Regardless, sampling data obtained using the NIOSH 7400 method should always stipulate which set of rules were used.

The limits for using PCM for fiber counts are the same as those encountered for asbestos counting. That is, the method is restricted by the practical limit of fiber resolution - about 0.25 Fm - 0.3 Fm in diameter (theoretical diameter resolution is about 0.15 Fm - 0.5 Fm). Scanning electron microscopy increases resolution to about 0.1 Fm, while TEM is needed to see smaller diameter fibers. This means that TEM will be required for reliable results when specifically sampling for fine and superfine fibers, using the NIOSH 7402 method for TEM (Manke *et al*., 1990; Roggli, 1991; Perrault *et al*., 1992).

A study by Rood and Streeter (1985) agrees that PCM is not an adequate technique for evaluating the special purpose MMVF exposures. Since these fibers typically have diameters less than 0.3 Fm, TEM must be used to get the resolution necessary to see the fibers. When Head and Wagg (1980) used PCM to analyze samples taken during installation of fine fiber products in aircraft, they reported that an average of 21% of the fibers had diameters under 1 Fm. Rood and Streeter reevaluated the samples using TEM and found that at least 85% of the insulation fibers were <1 Fm in diameter.

While polarized light microscopy (PLM) can be used for some MMVF identification, most of the available data recommends using SEM or TEM. X-ray diffraction is required for positive identification of fine fibers.

It should also be noted that several studies have collected and analyzed MMVF using side-by-side comparisons of the gravimetric and fiber counting methods (Corn and Sansone, 1974; Konzen, 1976; Esmen *et al.*, 1979a; Friar and Phillips, 1989; Perrault *et al*., 1992). Data shows that there is no correlation between samples collected by the two methods. Fiber counts cannot be reliably estimated from gravimetric analyses, nor does total weight give any indication of the number of fibers present. Further, fiber measurements and composition of the bulk products are not representative of the size or composition of the airborne fibers generated.

Brown (1992) studied twenty commercially available MMVF products manufactured from 1969-1988, including glass wool, rock wool, glass fiber strands and ceramic fibers. Samples for sizing were prepared by either: (1) teasing tufts of bulk material till they were evenly distributed; (2) making a slurry of ground tufts of bulk insulation; or (3) collecting airborne samples during simulated work operations. He concluded that fiber size distribution of bulk material is not representative of airborne fiber distributions during work unless the bulk material is first subjected to some means of mechanical breakdown.

Automated Methods

Automated sampling methods were developed especially for the asbestos industry, and the MMVF literature does not address analyses using automated counters. Thus, the accuracy and reliability in assessing vitreous fibers are unknown.

OSHA (1984) refers to an automated fibrous aerosol counter for screening airborne fiber exposures. Note that this is a screening method only, and is not valid for compliance purposes. The counter uses a helium-neon laser and optical sensors to detect fiber oscillations as the aerosol passes through a high intensity electrical field. Phanprasit *et al.* (1988) reported good correlation between fiber counts obtained with the NIOSH 7400 PCM method (B rules) and with the model FAM-1 (GCA Corporation) aerosol monitor. The FAM manufacturer lists minimum detectable fiber diameter as 0.2 Fm, with a length range of 2-200 Fm. Fiber aspect ratio can be set by adjusting the threshold value of the detector.

Automated microscope counters are also available. Baron and Shulman (1987) studied one such counter and concluded that it was at least as accurate for fiber counting as the manual method.

STANDARDS AND RECOMMENDATIONS

OCCUPATIONAL STANDARDS

Required Exposure Limits

Navy Occupational Safety and Health (NAVOSH) standards are based on the hierarchical adoption or incorporation of existing laws and standards as defined in chapter 16 of OPNAVINST 5100.23 series (CNO, 1994). NAVOSH permissible exposure limits (PELs) for the man-made vitreous fibers are listed below. All are 8-hour time weighted averages (8-hr. TWA).

Fibrous glass dust (CAS* 65997-17-3; RTECS* LK3651000) - 10 mg/m³

Mineral wool fiber (RTECS PY8070000) - 10 mg/m³
NOTE: Value is for inhalable [total] particulate matter containing no asbestos and <1% crystalline silica.

Refractory ceramic fiber (CAS 142844-00-6 as RCF; RTECS BD1450000 as aluminum III silicate) - 15 mg/m³, total dust; 5 mg/m³, respirable fraction
NOTE: Regulated as "Particulates not otherwise regulated."

These standards apply for "pure" product exposures at all Navy facilities (i.e., if MMVF insulation being removed is contaminated with asbestos, then the more stringent exposure limits [asbestos] take precedence). Should the manufacturer's material safety data sheet (MSDS) list other exposure limits, the industrial hygienist (IH) must assess the scientific validity of the limits. Remember that exposure guidelines from manufacturers may not always be based solely on concern about human health risk. You will also find that MMVF MSDSs usually have exposure limits listed in fibers per cubic centimeter (f/cc). This presents a problem since there is no direct correlation between gravimetric and fiber count results, as addressed in the section on sampling and analysis.

After-service refractory ceramic fiber products used in high temperature applications (>1000EC) may contain cristobalite (CAS 14464-46-1). Cristobalite is regulated by OSHA as crystalline silica, with the PEL calculated based on the percent of silica present (OSHA, 1997). The ACGIH TLV® for cristobalite is 0.05 mg/m³ (respirable dust) (ACGIH, 1997). The International Agency for Research on Cancer (IARC) recently upgraded crystalline silica from Group 2A (probably carcinogenic to humans) to Group 1 (carcinogenic to humans) (IARC, 1996).

Recommended Exposure Limits

It is important to discuss other MMVF standards and guidelines, both to look at historical perspectives and to gain an appreciation for concerns discussed along the way. NIOSH published

* CAS - Chemical Abstract Service (CAS, 1997)
RTECS - Registry of Toxic Effects of Chemical Substances (RTECS, 1997)

the first MMVF exposure limit, with a recommended exposure limit - or REL -for fibrous glass. The REL was 3 f/cc (#3.5 Fm diameter and $10 Fm long) with a 5 mg/m³ total fibrous glass limit. The gravimetric standard was intended to cover the larger fibrous glass fraction associated with mechanical irritation effects (NIOSH, 1977a).

From 1985 to 1987, Naval Sea Systems Command and Naval Medical Command (now Bureau of Medicine and Surgery) addressed the lack of consensus on long range health impacts of MMVF and the concern that there was no Navy PEL for man-made fiber exposures (e.g., NAVMEDCOM, 1986, 1987; NAVSEASYSCOM, 1985, 1986a, 1986b). After several years, data from literature searches, toxicological evaluations and other assessments led NAVMEDCOM to state that, although it had not been proven that MMVF were as hazardous as asbestos, control procedures should be the same. Further, they endorsed a standard of 2 f/cc for all MMVF, based on manufacturer recommendations and NIOSH endorsements. These recommendations were eventually incorporated into the Naval Ships' Technical Manual for insulation, with a 2 f/cc PEL for fibrous glass, mineral (rock or slag) wool, and ceramic fibers, and a total dust PEL of 10 mg/m³ for calcium and magnesium silicate dusts (NAVSEASYSCOM, 1990). Later updates of the manual removed these values, referring the reader instead to the current OPNAV instructions [OPNAVINST 5100.23 Series, Navy Occupational Safety and Health Program Manual; OPNAVINST 5100.19 Series, Navy Occupational Safety and Health Program Manual for Forces Afloat] (NAVSEASYSCOM, 1995).

In 1992, OSHA proposed a 1 f/cc PEL (8-hr. TWA) for "respirable fibers of fibrous glass, including refractory ceramic fibers." The PEL was to apply to general industry, construction, maritime and agriculture. OSHA postponed the hearings and indefinitely extended the comment period following legal controversy and the court's overturning of PELs issued using similar "blanket" adoption procedures (OSHA, 1992a, 1992b).

In their comments on OSHA's proposal, the trade unions for building and construction recommended that the RCF PEL be established at 0.1 f/cc, but otherwise agreed with OSHA's proposal of 1.0 f/cc PEL for all other MMVF (as 8-hour TWAs) and with the dust PEL for continuous glass. They further suggested that these PELs be added to the construction standards, and that NIOSH be tasked to do additional work on MMVF exposure characterization in the construction trades (Kojola and Moran, 1992).

In 1996, ACGIH listed synthetic vitreous fibers (SVF) in the Notice of Intended Changes for Threshold Limit Values® (TLVs®). In May 1997, the ACGIH voted to move the following proposed TLVs® to the adopted TLV®-TWA listing:

1 f/cc - continuous filament glass fibers; glass wool fibers; rock wool fibers; slag wool fibers; special purpose glass fibers (fiber defined as diameter < 3 Fm, length >5 Fm with aspect ratio >5:1, as determined by the membrane filter method at 400-450X magnification, phase contrast illumination)

5 mg/m³ - continuous filament glass fibers, inhalable fraction

The TLV® for refractory ceramic fibers remains on the 1997 Notice of Intended Changes, with a comment that the TLV® is still under review.

Always check MMVF product MSDSs to see if there are other chemicals that are regulated (i.e., from binders or sizings added during manufacture). If so, you must meet these PELs in addition to those for the fibrous component. Below are some sample manufacturer recommendations:

Owens-Corning (Owens-Corning, 1994) - fiber glass - 5 mg/m³, respirable
synthetic calcium silicate - 5 mg/m³, respirable
crystalline silica - 0.1 mg/m³, respirable

Manville (Manville, 1990, 1997) - fibrous glass, continuous filament - 1 f/cc
fiberglass wools - 1 f/cc
refractory ceramic fiber - 1 f/cc
crystalline silica (cristobalite) - 0.1 mg/m³

Carborundum (Carborundum Company, 1994a) - refractory ceramic fibers - 1 f/cc

For comparison, the following shows how other countries regulate MMVF (compiled from IARC, 1988; Friar and Phillips, 1989; Rindel *et al*., 1989; ILO, 1990; Kojola and Moran, 1992; OSHA, 1992a). All are 8-hr. TWAs unless otherwise noted.

Australia - synthetic mineral fibers - 0.5 f/cc
Austria - total dust - 10 mg/m³
lists superfine fibers as suspect carcinogen
Canada - glass, rock and slag wool - 1 f/cc
refractory ceramic fibers - 0.5 f/cc
Denmark - man made mineral fibers - 1 f/cc
glass wool - 2 f/cc (stationary work places)
5 mg/m³ (non-stationary work places, total dust)
Finland - glass wool and mineral wool - 10 mg/m³
France - general dust, mineral wool - 10 mg/m³
Germany - synthetic vitreous fibers - 0.5 f/cc
Great Britain - synthetic mineral fibers - 1 f/cc
total dust - 5 mg/m³
Netherlands - glass wool, glass microfibers - 3 f/cc
refractory ceramic fibers - 1 f/cc
New Zealand - synthetic mineral fibers - 1 f/cc
Norway - man-made mineral fiber, synthetic mineral fiber - 1 f/cc
Poland - glass wool - 2 f/cc
total dust - 4 mg/m³
Sweden - synthetic inorganic fibers, respirable - 1 f/cc
USSR - glass dust or fibers - 2 mg/m³

lists superfine fibers as suspect carcinogen

Other Exposure Classifications

The carcinogenicity (ability to induce cancer), fibrogenicity (ability to induce fibrosis) and cytotoxicity (ability to cause cell damage or death) of MMVF have been evaluated and classified by several groups. Their findings are summarized below.

IARC (IARC, 1988)

Glass wool - Group 2B, possibly carcinogenic to humans (based on sufficient animal evidence and inadequate human evidence)

Glass filaments - Group 3, not classifiable as to carcinogenicity to humans (based on inadequate animal evidence and inadequate human evidence)

Rock wool - Group 2B, possibly carcinogenic to humans (based on limited evidence in animals and limited evidence in humans)

Slag wool - Group 2B, possibly carcinogenic to humans (based on inadequate evidence in animals and limited evidence in humans)

Ceramic fibers - Group 2B, possibly carcinogenic to humans (based on sufficient evidence in animals and no data available for humans)

Silica (cristobalite) - Group 1, carcinogenic to humans (IARC, 1987, 1996)

EPA (Vu, 1988, 1994; IRIS, 1997)

Glass fiber - No group classification. Overall, inadequate evidence of carcinogenicity for glass filaments, glass wool and small diameter glass. Glass microfiber is cytotoxic and causes chromosomal aberrations.

Rock/slag wool - No group classification. Inadequate evidence of carcinogenicity and fibrogenicity.

Ceramic fibers (aluminosilicates) - Group B2, probable human carcinogen (sufficient evidence in animals and inadequate or no evidence in humans). Sufficient evidence for fibrogenicity.

EPA includes MMVF on their Master Testing List, used to establish testing needs and priorities for substances of concern that have not been adequately evaluated for human health impact.

NTP (NTP, 1994)

Glasswool (respirable size) - May reasonably be anticipated to be a carcinogen (based on sufficient evidence in animals).

Ceramic fibers (respirable size) - May reasonably be anticipated to be a carcinogen (based on sufficient evidence in animals).

OSHA has also issued clarification that fibrous glass product labels must include a warning about the possible cancer hazard from inhalation. Their statement was the result of an inquiry on how to meet hazard communication standard warning requirements (BNA, 1991).

ACGIH (ACGIH, 1997)

Continuous filament glass fibers - A4, Not Classifiable as a Human Carcinogen

Glass wool fibers - A3, Animal Carcinogen

Rock wool and slag wool fibers - A3, Animal Carcinogen

Special purpose glass fibers - A3, Animal Carcinogen

Refractory ceramic fibers - A2, Suspected Human Carcinogen.

ENVIRONMENTAL STANDARDS

Man-made vitreous fiber materials are not currently regulated as hazardous waste (HW). Debris should be wetted to avoid creating airborne dust/fibers, placed in heavy plastic bags or other suitable containers, and disposed of in approved sanitary landfills per local, state and federal regulations. If the MMVF is contaminated with any substance that is classified as HW (e.g., toxic, corrosive or reactive contaminants), disposal should be in accordance with the requirements for the contaminant(s).

In 1994, the Environmental Protection Agency (EPA) proposed a significant new use rule (SNUR) for RCF whereby notification is required before "...commencing the manufacture, import, or processing of refractory ceramic fiber (RCF) in any new product form or any new application of an existing product form" (EPA, 1994a). The issue was reopened for discussion (EPA, 1994b), but the SNUR for RCF is not yet published in the CFR as proposed for subpart 721.2090, "Refractory Ceramic Fiber (EPA, 1996 [40 CFR Part 721]).

As part of the Testing Consent Order between EPA and the Refractory Ceramic Fiber Coalition (RCFC), anyone exporting RCF must comply with notification requirements under section 12(b)(1) of the Toxic Substances Control Act (TSCA) and 40 CFR Part 707 (EPA, 1993). RCF testing is specifically listed by EPA (EPA, 1996 [40 CFR Part 799.5000]).

Other EPA regulations include:

Standards of performance for glass manufacturing plants (EPA, 1996 [40 CFR 60.290-296])

Maximum allowable emission of grams (g) particulate per kilogram (kg) glass produced, applicable to wool fiberglass in glass melting furnaces - Gaseous fuel fired - 0.25 g/kg
Liquid fuel fired - 0.325 g/kg
Modified processes - 0.5 g/kg

Standard of performance for wool fiberglass insulation manufacturing plants (EPA, 1996 [40 CFR 60.680-685])

Rotary spin wool fiberglass insulation manufacturing line - particulate emission not to exceed 5.5 kg/Mg (11.0 pounds/ton) of glass pulled.

EPA also lists effluent guidelines for glass manufacturing point sources (EPA, 1996 [40 CFR 426]).

PERSONAL PROTECTIVE EQUIPMENT AND ENGINEERING CONTROLS

Controlling airborne fiber generation can be accomplished in several ways. As always, engineering controls are preferable. In the case of man-made vitreous fibers, using good housekeeping practices and promoting personal hygiene will go a long way towards protecting personnel.

The following information is compiled from manufacturer's material safety data sheets, product literature, and information bulletins (e. g., Carborundum Company, 1991; Manville, 1990, 1997; Bender, *et. al.*, 1991). MMVF operations should be evaluated by an industrial hygienist, including valid air sampling data. Industrial hygiene will recommend engineering controls and PPE based on their assessment.

Engineering Controls

Tools used for machining operations on man-made vitreous fiber products (i.e., saws, drills, grinders) should be equipped with local exhaust to collect dusts and fibers at the generation point. Whenever possible, use non-power hand tools. Wet methods will also help to keep dust generation low. Provide containments for removal operations, including the use of glove bags where applicable.

Personal Protective Equipment

The following personal protective equipment is recommended:

Skin protection. Wear loose, long sleeved clothing closed at the neck and wrists, head covering, and gloves. Non-disposable coveralls should be thoroughly vacuumed before leaving the work area. Always wash reusable clothing separately from other clothing before wearing again.

Eye protection. Wear safety glasses or goggles with side shields to protect against eye irritation. This is especially important when the work operation is likely to generate falling debris (e.g., overhead insulation installation or removal) or dusty conditions (blowing insulation).

Respiratory protection. Respiratory protection may be warranted based on air sampling data. Examples of operations likely to result in exposures above the PEL include: after-service refractory ceramic fiber removal (fibers, dust and cristobalite); loose fill insulation installation; using power tools on MMVF; and any work in confined or poorly ventilated spaces. Consult the MSDS for the MMVF material for additional recommendations on respiratory protection.

Dust respirators may be needed to protect personnel in the work area from experiencing upper respiratory discomfort - scratchiness, irritation, or burning in the throat and/or nose. Remember that anyone wearing respiratory protection must be fully enrolled in the command's respiratory protection program.

Hygiene and Housekeeping

To prevent skin irritation, personnel should always wash thoroughly with soap and water before breaks and at the end of the work shift. Showering at the end of the work shift is recommended. Do not allow eating, drinking, or smoking in the work area.

Should skin irritation occur, instruct personnel not to scratch or rub the affected area. This may cause the fibers to penetrate even deeper into the skin. Remove clothing, wash the area with warm, soapy water and rinse thoroughly.

Any MMVF insulation scraps that fall during work should be picked up as soon as possible. This will keep workers from walking on the material and crushing fibers into smaller pieces that could more easily become airborne.

As a minimum, the work area should be vacuumed at the end of the work day. HEPA vacuuming is recommended.

FIBER MORPHOLOGY, DEPOSITION AND CLEARANCE

Knowledge of fiber morphology, deposition and durability is crucial to understanding the concerns about man-made vitreous fibers. To begin with, fibers must have the proper aerodynamic dimensions to be inhaled. If inhaled, they are of concern if they reach the alveoli and are deposited. The critical factor then becomes whether alveolar macrophages can effectively phagocytize or translocate the fiber. If not, the fiber's ability to resist dissolving determines if it will be retained long enough to elicit a biological response. McClellan and Hesterberg (1994) summarized these issues nicely when they defined biopersistence. During discussion at a meeting of the International Agency for Research on Cancer, they said it is "the retention in the lung, over time, of fibers with regard to number, dimensions, specific surface area, surface structure and chemistry, chemical composition, and similar characteristics. Changes in any of these parameters may alter fiber toxicity."

Numerous studies have cited fiber diameter as the most important morphological feature of respirability (Timbrell, 1965; Stanton, 1973; Kotin, 1978; Timbrell, 1982; Hesterberg and Barrett, 1984). Fibers with diameters greater than about 5 Fm will lodge in the nose. If the diameter is between 3 and 5 microns, the fiber can enter the trachea but does not usually penetrate deeply enough to be retained in the lung. In fact, much of the material in the upper respiratory system is effectively removed by the mucociliary escalator.

Fiber penetration into the deep lung occurs when diameters are less than about 3 Fm. This is the generally accepted upper limit of respirability (Esmen *et al.*, 1978; WHO, 1985), although 3.5 Fm has also been used (NIOSH, 1977a; IARC, 1988).

Fiber respirability and retention has also been studied in relation to fiber length. The consensus is that fibers less than about 200-250 Fm should be considered respirable (Timbrell, 1965; Kotin, 1978; Timbrell, 1982), but fibers longer than about 5 Fm are less likely to be deposited in the alveoli (Harris and Timbrell, 1977; Morgan *et al*., 1980; Hammad *et al*., 1982; Morgan *et al*., 1982).

Should long fibers reach the deep lung, macrophage translocation may be ineffective in removing them, depending on the length. Morgan (1980) reported that the macrophage plasma membrane is damaged when it engulfs fibers longer than about 10 Fm, thereby preventing removal. Fibers may even pierce and project through the macrophage's cell wall, causing the macrophage to become lodged as it moves intracellularly. Morgan and Holmes (1984) state that the clearance seems to remain impaired up to about 30 Fm. More recent studies indicate that fibers equal to or longer than the size of lung macrophages - about 15 Fm - may indeed be linked to the biological effects (McConnell, 1994; Morgan *et al*., 1994).

Luoto *et al*. (1994) studied rates of alveolar macrophage (AM) phagocitization and AM morphological changes after exposure to rock wool (70% fibers <1 Fm diameter). They observed several interesting occurrences: phagocytosis began within 30 minutes of exposure; two or more macrophages often simultaneously engulfed single long fibers; and AMs would attach to fibers regardless of whether or not they

had already ingested a fiber. The maximum fiber length that a single macrophage could successfully engulf was about 20 Fm.

In general, then, the possibility of alveolar deposition increases as the diameter and length decrease. If the fiber is deposited, its biological activity becomes dependent on durability. Studies have shown that fibers in the lung get smaller, break, undergo surface etching and become coated with gelatinous proteins over time. It has been hypothesized that a fiber's biopersistence may be the driving factor in its ability to cause tumors. That is, if fibers remain in contact with lung cells long enough, they can create a cumulative dose high enough to induce pathogenic effects. Conversely, if the fibers dissolve relatively easily, they will not reach the threshold needed to cause adverse effects. Indeed, chronic cellular injury from biopersistent fibers appears to be key factor in fiber-associated fibrosis and cancer (Everitt, 1994).

Fibrous glass dissolution was followed by Bellman *et al*. (1986) and Morgan *et al*. (1982). Their work concluded that fibers dissolve at rates dependent on their length. Shorter fibers (5-10 Fm) dissolve more slowly and uniformly than do longer fibers (30-60 Fm). However, shorter fibers have a much faster clearance rate from the lung, presumably due to macrophage intervention (Morgan, 1980; Johnson *et al*., 1984; Morgan and Holmes, 1984; Bellman *et al.*, 1986). Thin fibers - less than 3 Fm in diameter - also degrade more rapidly than do coarse fibers (Spurny *et al.*, 1983).

Similar work by Muhle *et al.* (1991) resulted in fibrous glass "half life" rankings: crocidolite - 1000 days; thick fibrous glass (90% < 2.49 Fm) - 107 days; thin glass (90% < 0.88 Fm) - 38 days; thin glass with low calcium oxide content - 238 days. Wollastonite, used as a known"short resident" fiber, had half life ratings of 10-12 days.

Scholze and Conradt (1987) established a durability classification by exposing natural and man-made fibers to a simulated extracellular fluid. They found that glass wool, superfine glass, and refractory silica fibers were about 50% dissolved after 4 months of exposure. Slag wool, refractory Fiberfrax®, chrysotile, and crocidolite showed less than 5% degradation in the same time period. Others report similar results, ranking MMVF solubilities, from most to least soluble: glass fibers, slag wool > rock wool > RCF > chrysotile > amphibole asbestos (Hammad, 1984; Law *et al*., 1990; McClellan *et al*., 1992).

In general, Leineweber (1984) agreed with the Scholze and Conradt findings. However, he tested one type of glass fiber that was extremely durable, leading him to conclude that the amount and chemical composition of the glass in the fibers was the major determinant in solubility rates.

Another study calculated dissolution lifetimes for 1 Fm diameter test fibers. In general, lifetimes for the natural fibers were over 100 years, whereas the MMVF group had lifetimes of less than 6.5 years. Within the vitreous fiber group, superfine glass, glass wool, slag wool, and refractory silica would dissolve in less than two years, with fine glass fibers dissolving in less than one year. Fiberfrax® and E glass wools take 5 to 6.5 years to degrade (Förster, 1984; Scholze and Conradt, 1987).

Glass fiber dissolution rates *in vitro* have been correlated with those *in vivo* by intratracheal instillation of glass fiber suspensions in rats, followed by periodic fiber counts and sizing up to one year post-injection.

Using five different glass samples, researchers found that the peak diameter of injected fibers longer than 20 Fm declined with time at the same rate as that found in *in vitro* studies (as measured in pH 7.4 simulated lung fluid) (Eastes et al., 1995).

Wagner *et al*. (1984) compared fiber retention of rock wool and asbestos in rats twelve months and 24 months after exposure to the fibers. The weight of rock wool decreased from 3.1 mg to 1.5 mg; asbestos weight was 0.42 mg at 12 months and 0.40 mg at 24 months. Cytological examinations showed that over time, the rock wool fiber surfaces were etching and the fibers changed shape. This was attributed to the leaching of the minerals as the fiber was dissolved by bodily fluids, with subsequent changes in surface porosity. These changes leave the fiber even more vulnerable to attack by the fluids. Similar results were obtained by Davis (1986), LeBouffant *et al*. (1987), and Hammad (1988).

Musselman *et al*. (1994) found that 90-100 % of glass and mineral wool fibers larger than 0.5 Fm diameter and 20 Fm long are cleared from rat lungs within 270 days post inhalation, whereas only about 60% of crocidolite fibers cleared. They tested several of the fibers being used in the Research and Consulting Company's long-term inhalation study, including MMVF 10 (Manville glass wool), MMVF 11 (Certainteed glass wool), MMVF 21 (Roxul rock wool) and MMVF 22 (USG slag wool). While the MMVF decreased in geometric mean diameter and length over time, crocidolite fibers recovered from the rat lungs remained essentially the same size. The authors concluded that the longer, thicker MMVF fibers dissolve or break over time, leaving the shorter thin fiber fractions (<0.5 Fm diameter x <5 Fm long).

MMVF 11 (glass wool), MMVF 22 (slag wool) and a single RCF sample were evaluated by Bauer *et al*. (1994). They looked at dissolution rates in pH 4, simulating intracellular environment after phagocytosis, and at pH 7.6, simulating extracellular fluid. Regardless of pH, the wools dissolved faster than the RCF, with the glass wool dissolving fastest at pH 7.6 and slag dissolving more quickly in the acidic environment.

Although most researchers agree that MMVF are much more soluble than asbestos, Bellman *et al.* (1987) found otherwise. Following a two year study of crocidolite, chrysotile, glass wool, five types of glass fibers, rock wool, and two kinds of ceramic fibers, they concluded that two of the glass fibers were at least as durable in the lung as crocidolite and that ceramic fibers were over four times as durable. It should be noted, however, that the ceramic fibers were much thicker, therefore required more time to dissolve than the other fibers.

Bernstein *et al*. (1995) evaluated MMVF biopersistence using an inhalation model. Aerosols of MMVF 11 (glass wool, geometric mean 0.76 Fm diameter x 12.67 Fm long), Fiber B (soluble glass fiber, geometric mean 0.48 Fm diameter x 11.20 Fm long) and Fiber J (synthetic stone wool, geometric mean 0.55 Fm diameter x 10.04 Fm long) were given to rats at 30 mg/m^3 for 5 days, 6 hours/day. Animals were held for one year, with interim sacrifices. Half lives ($T_{1/2}$) for MMVF 11, Fiber B and Fiber J were 20, 5 and 7 days, respectively. Fibers broke and disintegrated quickly in the lung, especially during the first 24 hours. Short fiber fractions had $T_{1/2}$ of 46, 10 and 12 days (11, B and J). Fiber diameters did not change significantly over time.

EXPOSURE DATA

ENVIRONMENTAL EXPOSURES

Data on environmental sampling is limited. In 1987, there was a study of buildings with in-place slag wool tiles and insulation. General area (GA) ambient air samples showed that fiber levels were below the limit of detection, which was 0.02 fibers per cubic centimeter (f/cc) (TIMA, 1990).

In their summary of MMVF exposures, McClellan *et al*. (1992) included a few environmental samples. Ambient samples had a mean concentration of 0.0026 f/cc. The mean range found inside schools and day care facilities was 0.000025-0.00026 f/cc. Samples taken inside air ducts showed mean fiber counts of 0.001 f/cc.

Ambient fibrous glass and glass lined ventilation duct fiber counts were reported by Balzer (1976). Samples taken over a 3½ year period showed ambient levels of none seen to 9.0 fibers per liter (f/L), with a mean fiber size of 4.3 Fm x 61.8 Fm. Inside ducts, fibers were a little smaller - 3.7Fm x 51.3 Fm - and fiber concentrations less - none seen to 2.0 f/L. [NOTE: To convert f/L to f/cc, divide f/L by 1000.]

Gaudichet *et al*. (1989) also sampled conditions inside buildings and ventilation ducts where MMVF materials were used in sprayed insulation, pipe coverings, ceiling panels, ventilation filters, etc. Samples were collected and analyzed using a modification of the procedure for atmospheric contamination by asbestos fibers. Samples are collected at 5 liters per minute (Lpm) during weekday work hours, yielding a total air volume of about 10 cubic meters (m^3). When counted, fibers # 3 Fm diameter were tallied as the respirable fraction. For 79 samples, results were: respirable fibers, inside - 0-6230 f/m^3; respirable fibers, outside - none detected-15 f/m^3; total fibers, inside - 0.2-6778 f/m^3; total fibers, outside - 0.3-22 f/m^3. [NOTE: To get f/cc, divide f/m^3 by 10^6.]

Responding to public perception that shedding fibers from ceiling materials were responsible for respiratory infections in kindergarten children, the Danish Board of Health initiated a study of school environments. Rindel *et al*. (1989) looked at 24 kindergartens, including about 900 children and 200 adults. The study included parent and employee questionnaires, clinical evaluations and air sampling. The sampling protocol covered airborne and settled dust analysis for fibers, as well as other parameters that were included because of the possibility of sick building syndrome.

Kindergartens were divided into three sample groups: Group A - MMVF ceiling materials with water soluble binders; Group B - MMVF ceiling materials with resin binders; Group C - control classes, no MMVF products readily visible. Each school was sampled three times during the 12-week study period. Fiber results are listed in Table 8. The authors found no correlation between symptoms or disease and MMVF exposure, nor were there any significant differences in mean concentrations of airborne respirable

fibers or of settled dust fibers across the three groups. There was a correlation in the adults between the fiber concentration and reported eye irritation, and between settled MMVF dust and skin irritation.

Table 8. Airborne and settled dust MMVF results in kindergartens

	Group MMVF Fiber Results		
Fiber Type	A	B	C
Airborne, non-respirable, f/m³	23	40	0-77
Airborne, respirable, f/m³	110	97	41
Settled, cleaned regularly, f/cm²	0-0.7	0-0.4	0-0.4
Settled, cleaned occasionally, f/cm²	0-11	0-120	0-5

OCCUPATIONAL EXPOSURES

Occupational exposures to MMVF can occur during manufacturing, packaging, installation or removal of any of the materials. Navy personnel encounter the latter two situations. It should be noted that, although the main concern about MMVF is the release of airborne respirable fibers, commercial products may contain chemical additives (lubricants, binders or sizings added during manufacture). This can only be determined by consulting material safety data sheet (MSDS), product literature or by contacting the manufacturer.

Ocular Exposure

The morphology of MMVF makes them excellent candidates for causing irritation. The sharp, broken ends of the fibers can actually penetrate tissues and cause various reactions. Fibers can reach the eye through airborne transmission or by transfer on the fingers or clothes. Lucas (1976) reported that eye irritation was common in fibrous glass workers, but posed no real health threat. The literature does not address ocular exposures again until 1982, when Stokholm *et al*. published a study on ophthalmological effects found in the rock wool industry. The survey included workers with at least six months exposure, and involved medical histories, questionnaire analysis, eye examinations and cytological analyses of conjunctival fluids. The report concluded that rock wool fibers cause ocular irritation, but it was reversible when the worker was removed from the environment, such as over the weekend.

Dermal Exposures

Transient dermatitis was attributed to man-made vitreous fiber exposures as early as the 1940s (Sulzberger *et al*., 1942). The inflammatory response is caused by actual fiber penetration and the associated release of histamines. Burning and itching are the usual symptoms. The degree of inflammation varies with the type of fiber, since size and stiffness are the predominant factors for fiber penetration. Although skin irritation has been reported for all the MMVF, it is apparently most common with fibrous glass, particularly if the diameter is $5 Fm (Possick *et al*., 1970; NIOSH, 1977a; TIMA, 1990). Fibers less than 1 Fm across will not cause irritation (Bender, Konzen and Devitt, 1991).

The irritation is usually relieved by washing the skin and ensuring that contaminated clothing is promptly removed. The dermal reactions may dissipate or even disappear with continuous exposure (Lockey, 1981). However, if there is a lapse in exposure, the response often recurs (Hill, 1980).

Upper Respiratory Irritation

Upper respiratory irritations, such as pharyngitis and rhinitis, have been reported, but are not common. The reaction is triggered by the same mechanical irritation that causes dermal effects, with burning and scratchiness of the nose and throat associated with the reaction. This is not an allergic reaction and generally does not persist. There are no reports of lung sensitization or pleural allergic reactions (Lockey, 1981; Manville, 1990; TIMA, 1990; Bender, Konzen and Devitt, 1991).

The real occupational exposure concern is lower respiratory fiber penetration. The ability of the fiber to be deposited and its durability were discussed in the fiber morphology section. The biological responses to lower respiratory exposure will be deferred until the toxicology discussion.

Inhalation Hazards

Occupational inhalation hazards must be assessed by collecting air samples and quantifying airborne fibers. Though the Navy is concerned with the installation and removal of MMVF materials, manufacturing data is included for comparison. Results may be given as concentrations, fiber counts, or both, depending on the methods used by the researcher.

When evaluating the fiber exposure results, keep in mind that the analytical methods are not the same for all the studies. Since the definition of a fiber and the rules for counting vary with the analytical method, results may not be directly comparable. In addition, early studies may have reported results using the P&CAM analytical method (NIOSH, 1977b) rather than the 7400 fiber counting method currently used (NIOSH, 1994).

The convention is to define a fiber as being >5 Fm long with an aspect ratio of $3:1 (NIOSH, 1984). Respirable fibers have a diameter #3-3.5 Fm (NIOSH, 1977a; Esmen *et al.*, 1978; WHO, 1985; IARC, 1988). It will be noted if other criteria is used in the reports.

The following sections review some exposure data collected from both manufacturers and end users. Data are separated into manufacturing and user, with each MMVF group discussed individually within the category. Note that results may be given in fibers per milliliter (f/ml) if the original work was reported in these units. Fibers per ml is equivalent to f/cc. [For reference, 1 ml = 1.000027 cc.]

Manufacturing Air Sample Data

Fibrous Glass

Ottery *et al.* (1984) reviewed results from 13 European MMVF manufacturing plants, with samples collected from 1977 to 1980. They reported that the respirable fiber concentrations in continuous filament plants averaged <0.01 fibers per milliliter (f/ml). Glass wool exposures averaged less than 0.1 f/ml. The highest levels, ranging from 0.08 f/ml to 1.89 f/ml, were found in the production of special purpose fine fibers.

This data was reanalyzed by Cherrie *et al.* (1986) using the World Health Organization analytical reference method (WHO, 1985). This method is essentially the same as the NIOSH 7400 with the A counting rules (NIOSH, 1994). Random samples from the Ottery *et al.* collection were recounted, and though the fiber concentrations did increase, they still averaged the same for the continuous filament and glass wool plants. The exposures in the special purpose glass increased to an average of 0.17 to 4.02 f/ml. The glass wool fibers were sized with scanning electron microscopy (SEM) at a median plant diameter of 0.7-1 Fm and length of 8-15 Fm.

A study of 16 MMVF plants in the United States showed that area mean exposures in the fibrous glass industry were 0.002 to 0.78 f/cc (Esmen *et al.*, 1979a). This included ranges of 0.002 to 0.04 f/cc for continuous fibers and 0.01 to 0.78 f/cc for loose glass. Note that two of the plants produced "fine glass," with diameters from about 0.05 Fm (very fine) to 6 Fm. Personal exposure concentrations were 0.1 to 0.3 f/cc for fibers greater than 5 Fm. The study included over 1100 samples from all areas of manufacturing, as well as packaging, maintenance, shipping and quality control. Analysis was done by optical microscopy, not phase contrast microscopy (PCM).

Information for five of the glass plants was updated by Hammad and Esmen (1984). Actual results ranged from 0.0090 - 4.38 f/cc, with mean concentrations < 0.5 f/cc. The single exception was in the quality control section of one plant, where the mean fiber concentration was 2.22 f/cc.

The data from these studies also correlated fiber diameter with fiber respirability. They concluded that 50-90% of the airborne fibers produced with fine diameter glass (nominal diameter <3 Fm) are respirable.

When the diameter increased to greater than 6 Fm, the percentage of respirable fibers dropped to less than 40% of the total airborne concentration. They also correlated fiber diameter with airborne concentration: airborne fiber counts decreased with increasing fiber diameter.

During their evaluation of composite material manufacturing, Antonsson and Runmark (1987) sampled fibrous glass sheet cutting operations. Personal dust sample mean concentration was reported at 2.0 mg/m³, with general area samples at 0.1 mg/m³. Fiber count means were 0.08 f/ml and <0.05 f/ml for personal and GA, respectively. They also found that machining continuous filament products did not produce respirable fibers, but did produce respirable dusts.

Data reported by Indulski *et al.* (1984) at a single continuous glass plant showed fiber counts of 0.075-1.02 f/cc (total dust 0.1-3.5 mg/m³). The median diameter of the airborne glass fibers was 3.40 Fm, with 42.5% #3 Fm diameter (respirable).

Other manufacturing data consistently shows low exposures (Head and Wagg, 1980; Esmen, 1984; TIMA, 1990) except in the production of fine glass. Corn and Sansone (1974) studied three fiberglass plants, where overall mean fiber concentrations for personal respirable samples ranged from 0.02 to 1.41 f/cc. The highest concentration, 3.16 f/cc, was found in fine glass production. Following an industry survey of MMVF production facilities, TIMA (1990) also reported the highest exposures for special purpose glass. The average concentration was 1.42 f/cc (77.3% of samples <1 f/cc). All other glass manufacturing was <0.25 f/cc.

Data in Table 9 were reported by Dement (1975). Samples were from six small diameter glass (<1 Fm) manufacturers, 4 large diameter plants and one manufacturer of glass reinforced products. Again, high fiber counts are apparent for small diameter glass.

Table 9. Summary of manufacturer data presented by Dement (1975)

	Fiber Counts (f/ml)		Total Dust (mg/m³)	
Glass Category (median fiber size)	No. Samples	Range	No. Samples	Range
Large diameter (1.1-4.3Fm diameter; 19-70 Fm long)	167	0.00-0.83	146	0.01-14.5
Small diameter (size not given)	123	0.1-44.1	61	0.1-2.0
Reinforced plastics (5 Fm diameter; 35 Fm long)	10	0.02-0.10	10	0.1-5.7

Head and Wagg (1980) summarized exposures for a variety of glass productions in the United Kingdom. Defining a fiber as >5 Fm long and less than 3 Fm diameter, they found respirable concentrations of 0-0.08 f/ml in continuous filament manufacturing, with total fibers ranging from <0.001-1.43 f/ml. Respirable glass wool exposures ranged from 0.003 to 1.10 f/ml. For special purpose fibers (0.1-3 Fm diameter), respirable sample results were 0.02-18.83 f/ml. Note that samples collected were representative of the operation (i.e., not all were 8-hr. TWAs) and included both general area and personal samples. Head and Wagg estimated that, overall for the plants evaluated, 60-80% of the fibers generated were <3 Fm in diameter.

Results of IH sampling at 15 Owens-Corning manufacturing plants from 1970 to 1976 were reported by Konzen (1976). Mean total fiber counts for glass wool, including fibers <5 Fm long, was 0.11-0.16 f/cc. Textile production means ranged from 0.13-0.37 f/cc. The highest results were found in the small diameter (1-4 Fm) manufacturing plants, where the mean fiber count was 0.38 f/cc.
TIMA (1990) and Christensen (1991) reported sampling data collected from 1985 to 1989 by TIMA glass manufacturers, including 1569 manufacturing samples and 443 occupational exposure samples. The overall exposure mean concentration for glass was 0.62 f/cc, with 90% of the results ranging from 0.01 to 1.28 f/cc (94.3% of all results were less than 1 f/cc; 97.4% were less than 3 f/cc). Data are summarized in Table 10.

Table 10. TIMA member data summary by glass type, 1985-1989

Type of Glass (average diameter)	Number of Samples	Mean Concentration, f/cc	% Total <1 f/cc	% Total <3 f/cc
Glass wool (3-15 Fm)	1032	0.11	98.9	99.5
Continuous filament (3-25 Fm)	189	0.03	100	--
Fine diameter (<1-3 Fm)	348	2.45	77.3	89.7

As in previously reported studies, the data indicate that fibrous glass exposure problems are primarily with the special purpose, fine diameter fibers. TIMA reported a recalculated exposure level of 1.42 f/cc for fine glass when two "extreme values considered outliers" were discounted. The recalculated mean concentration for glass overall dropped to 0.39 f/cc.

Krantz (1988) reported exposure data from 10 Swedish factories, including glass wool, continuous filament glass and special purpose glass (for manufacturing ear plugs). The continuous glass plant was dropped from the study because no airborne respirable fibers were found in the pilot study. Samples were taken

on process worker, maintenance and cleaning personnel for the remaining 9 plants. Respirable glass wool results ranged from 0.01-1.8 f/cc (mean 0.18 f/cc), with a total dust mean of 1.9 mg/m^3. Respirable special purpose glass samples ranged from 0.08-2.4 f/cc (mean 0.47 f/cc), with a 1.0 mg/m^3 mean total dust. The authors note that no binders or lubricants were used in the special purpose plant. The highest exposures were documented during raw material handling.

Jacob *et al*. (1993) sampled various operations during manufacture of Owens-Corning Fiberglas® products. Analysis was done using the NIOSH 7400 method, and counted using both A and B rules. Sampling sites were selected to represent worse-case fiber concentrations. Results, shown in Table 11, are for length of operation, are not blank corrected and show filter plus cowl fiber counts (authors found significant fiber deposition on the cowls).

Table 11. Fibrous glass operations reported by Jacob *et al.* (1993). Results are arithmetic mean airborne fiber concentrations in f/cc. Number of samples taken is shown in parentheses.

Operation	7400 A Results, Total Fibers (No. samples)	7400 A Results, Glass Fibers Only (No. samples)	7400 B Results, Respirable Fibers (No. samples)	7400 B Results, Respirable Glass Fibers (No. samples)
Equipment insulation fabrication	0.026 (8)	0.009	0.007 (4)	0.001
Molding media	0.028 (31)	0.012	0.012 (16)	0.008
Fabrication press operation	0.20 (24)	0.14	0.087 (12)	0.071
Fabrication, other	0.038 (12)	0.015	0.007 (6)	0.002
Metal building insulation	0.043 (31)	0. 017	0.017 (16)	0.009
Manufactured housing	0. 019 (20)	0.080	0.032 (8)	0.019
Pipe insulation	0.20 (15)	0.052	0.055 (8)	0.020
Range assembly	0.058 (25)	0.039	0.029 (11)	0.023
Range assembly, wool unloader only	0.16 (2)	0.078	0.12 (1)	0.10
Duct assembly	0.038 (12)	0.009	0.008 (6)	0.005
Water heater assembly	0.047 (11)	0.030	0.022 (6)	0.018
Flex duct assembly	0.073 (62)	0.037	0.029 (31)	0.022

Rock Wool and Slag Wool

The Head and Wagg (1980) study of United Kingdom manufacturing plants also included rock and slag wool exposure samples. The respirable range for production processes was 0.03-10.3 f/ml, with personal and general area sampling data combined.

United States manufacturing data by Esmen *et al*. (1979a) included three slag wool plants, one rock wool plant and one plant that produced both. Mean fiber concentrations for slag wool ranged from 0.02 to 0.11 f/cc. The rock wool plant overall mean was 0.34 f/cc, while the plant manufacturing both wools yielded 0.10 f/cc. Recall that this data was obtained with optical microscopy.

Ottery *et al*. (1984) found total fiber exposures in six rock wool plants ranged from 0.004 to 2.00 f/cc, with respirable fibers <0.01-1.2 f/cc. Total gravimetric dust samples were 0.01-25.91 mg/m³. When a portion of the samples was reassessed by Cherrie *et al*. (1986) using the WHO (1985) reference method, results overall increased by a factor of 1.8. Sized by SEM, the rock wool fibers had median diameters of 1.2-2 Fm and lengths from 10 to 20 Fm.

Corn *et al*. (1976) studied exposures at a mineral wool and a slag wool plant, where average airborne fiber concentrations varied from 0.01 to 0.43 f/cc for slag and from 0.20-1.4 f/cc for rock wool. PCM analysis showed that 50-90% of the total particulate collected was <3 Fm in diameter and 60-90% was >10 Fm in length.

Personal exposures were monitored by Esmen *et al*. (1978) at five plants operated by different companies. Results ranged from 0.002 f/mm to 1.72 f/mm (data not available for conversion to f/cc). The highest exposures were found among janitorial and quality control personnel.

Swedish rock wool and special purpose rock fiber production plant exposures were reported by Krantz (1988). Respirable rock wool was 0.01-2.6 f/cc (mean 0.20 f/cc) with a 1.4 mg/m^3 mean total dust. Respirable special purpose samples were 0.45-1.9 f/cc (mean 1.4 f/cc), total dust mean 2.0 mg/m^3.

Area samples in three rock wool plants showed exposures ranged from 0.10-0.93 f/cc (0.3-6.0 mg/m³). The median size of the airborne fibers was 1.35-2.2 Fm in diameter and 10.0-41.0 Fm in length, with up to 84% being respirable (<3 Fm diameter) (Indulski *et al*., 1984).

TIMA (1990) reports data collected from 20 rock and slag wool plants. This information includes 1100 samples collected from 1987 to 1990 from three different manufacturers. Sample result ranges, separated by manufacturer, were: manufacturer A - 0.01-0.28 f/cc; manufacturer B - 0.02-1.59 f/cc; manufacturer C - <0.01-0.74 f/cc.

Refractory Ceramic Fibers

Data on ceramic fiber exposures was limited until recently. Under the auspices of the Refractory Ceramic Fiber Coalition (RCFC), RCF manufacturers instituted a Product Stewardship Program, which included expanding the exposure information base. Early on, data showed exposures to be higher than those found in the fine glass industry. For example, Friar and Phillips (1989) conducted a two year survey of ceramic fiber exposures in the United Kingdom. Typical manufacturing data included an array of samples, from chopping and baling raw fibers to mixing and needle operations. The lowest values were obtained in the product packing area - 0.02 f/ml. The highest results, 1.2 f/ml, were seen when chopping and bagging the raw fibers.

Esmen *et al.* (1979b) investigated three RCF production plants and reported an average exposure of 0.05 to 2.0 f/cc. Although the plants had operational differences, the airborne fiber sizes intraplant stayed relatively constant. About 95% of the total airborne fibers were less than 4 Fm diameter and 50 Fm long. Actual respirable fiber concentrations ranged from 0.02 to 6.9 f/cc for all plants. The highest value was found in an unventilated space during cutting, drilling and packaging.

Exposures to ceramic fibers were included in the United Kingdom manufacturer's study by Head and Wagg (1980). Mean respirable fiber counts were 0.03-6.14 f/ml.

Data gathered by TIMA (1990) from 1985 to 1989 shows a mean concentration of 0.65 f/cc for 1152 manufacturing samples, with 79.2 % of the samples <1 f/cc and 97.5% <3 f/cc. Analysis by SEM showed mean fiber dimensions of 1.4 Fm diameter and 25.8 Fm long.

In May 1993, RCFC members and EPA signed a Testing Consent Order for RCF under the Toxic Substances Control Act (EPA, 1993). Basically, the agreement stated that air monitoring data would be collected for eight functional job categories in both manufacturing and end user scenarios over a period of five years. The collected data, reported to EPA every six months, will be used to help make future decisions on RCF regulation. The sampling protocol also provides for monitoring silica during after-service removals in ovens and furnaces.

Table 12 summarizes data from the first full year of monitoring, which covers 877 samples. All results are 8-hr. TWAs (Carborundum Company Fibers Division, 1995). The overall decreasing exposure trend is attributed to using revised workplace practices and equipment/engineering controls recommended through the RCFC Product Stewardship Program.

Installation/Removal Air Sampling Data

Fibrous Glass

There are several studies documenting exposures during MMVF use, particularly during insulation installation. Fowler *et al.* (1971) sampled fiberglass insulating operations and obtained total fiber counts

of 0.5-8.0 f/cc (length of operation). The parent glass had mean diameters of 4 -10.2 Fm; operation fiber diameters ranged from 2.2 to 8.4 Fm. The authors estimated that 50% of the airborne fibers generated during installation were <3.5 Fm diameter.

Similarly, Schneider (1979) sampled insulation installers at 24 work sites during peak exposures. Respirable fiber levels were 0.011-3.5 f/cc, with about 50% of the fibers generated having diameters less than 1 Fm. The lowest exposures were found when installing insulation in prefabricated housing, while the highest exposures were recorded during pipe and existing structure insulation. Jacob *et al*. (1993) monitored work sites and found that glass wool duct board installers had mean total fiber exposures of 0.022 f/cc, and 0.002 f/cc for glass only. Pipe and ceiling insulation removal results were similar: total fibers - 0.29 f/cc; glass fibers only - 0.10 f/cc.

Table 12. Summary of RCFC data collected June 93 - June 94. Represents 474 customer workplace samples and 403 primary RCF manufacturing facility samples (Carborundum Company Fibers Division, 1995)

Work Category	Average Exposure, Baseline, f/cc	Average Exposure, First Year, f/cc	% Change
Fiber manufacture* (bulk and blanket production by primary producer)	0.384	0.192	-50
Assembly (combining RCF with other components, including furnace fabrication)	0.286	0.281	-1.7
Auxiliary Operations (passive RCF exposures during work, e.g., warehouse workers)	1.100	0.202	-81.6
Finishing (cutting/machining RCF after manufacture)	1.573	1.257	-20.1
Installation (construction/maintenance of industrial furnace linings)	0.694	0.567	-18.3
Mixing/Forming (wet production of RCF cast shapes and materials)	0.412	0.250	-39.3
Other, not elsewhere classified (e.g., die cutting, wrapping operations)	0.384	0.356	-7.3
Removal (after service)	1.359	1.267	-6.8
OVERALL WEIGHTED AVERAGE	0.70	0.495	-30.0

* Fiber manufacturing is the ONLY category for primary production. Other categories include data from both primary manufacturers and customers (secondary production and/or end users).

Head and Wagg (1980) reported that respirable fiber levels ranged from 0.24-1.76 f/ml when glass wool batting was installed in lofts. An estimated 66% of total airborne fibers were respirable. Similar results were reported by Balzer (1976), with exposures of 0.0005-2.407 f/cc. However, he estimated that only 15% of the fibers generated were respirable. Mean fiber dimensions were 6.5 Fm x 103.6 Fm. End user data collected by TIMA (1990) shows a mean exposure of 0.25 f/cc, with 93% of the values <1 f/cc and 99.5% <3 f/cc.

In 1982, Esmen *et al.* published results for home and aircraft insulating operations. The highest respirable results were seen with blown attic insulation. During this operation, an estimated 44% of the total fibers were respirable, with exposures of 0.67 to 4.8 f/cc for the length of operation. The length of operation mean, 1.8 f/cc, decreased to 0.78 f/cc when exposures were time weighted for an 8-hour exposure. Other home and commercial exposure levels varied from a mean respirable concentration of 0.0028 f/cc for acoustical ceiling tile installation to 0.13 f/cc for a building insulation operation.

Aircraft insulation operations yielded overall higher exposures, ranging from 0.05 to 3.78 f/cc. The fibers used for this application were <1 Fm diameter. The highest exposure was documented while cutting fiberglass blankets, where approximately 99% of the fibers generated were respirable.

Fibrous glass insulation operations, both batt and loosefill, were monitored during new residential construction by Lees (1991). He reports mean respirable TWAs as follows (actual sample result ranges in parentheses): batt installation - 0.15 f/cc (0.04-0.34 f/cc); loosefill with binder, installer - 0.53 f/cc (0.18-1.20 f/cc), feeder - 0.19 f/cc (0.06-0.69 f/cc); and loosefill without binder, installer - 7.40 f/cc (1.36-18.4 f/cc), feeder 1.82 f/cc (0.06-9.36 f/cc). Notice the marked increase in exposure values when loosefill insulation does not have a binder.

Jaffrey (1990) conducted sampling during a simulated do-it-yourself loft insulation. Analysis of the 250 samples was done by transmission electron microscopy (TEM), with fibers counted only if they were 5-100 Fm long and <3 Fm in diameter. Installers were not professional and were not given instructions beyond reading the manufacturer's literature. Both blown and blanket installations were sampled. General area respirable samples in the loft were <0.1 f/ml, compared with ambient levels of <0.002 f/ml. Personal samples were all <1 f/ml (range 0.15-0.67 f/ml), except during fine fibrous glass blanket installation, where the highest exposure recorded 1.76 f/ml.

Jaffrey *et al.* (1990) staged insulation disturbances intended to simulate routine building maintenance. The highest fiber counts during "minor" disturbance - moving boxes in insulated areas - was 0.11 f/cc. The major disturbance simulation, where insulation was beaten and lifted, yielded only slightly higher exposures at 0.20 f/cc. All analysis was done by TEM.

Five MMVF work sites were monitored by Perrault *et al*. (1992). The authors used WHO (1985) rules for phase contrast optical microscopy (PCOM) to count fibers and TEM for determining fiber size distributions and bulk composition. All samples were general area. One operation involved glass wool panel installation; another was RCF blanket and glass wool panel installation. For the glass wool only, geometric average concentration was 0.01 f/cc and bulk fibers were sized at geometric average 0.50 Fm diameter, 2.9 Fm long. In the RCF/glass wool operation, results were 0.04 f/cc, bulk material 0.71 Fm x 13 Fm.

Lees *et al*. (1993) conducted one of the most complete user exposure surveys reported. They monitored workers during insulation operations in 107 houses in 11 different states, sampling by work operation groups. Fiber counts were done using both phase contrast microscopy (PCM) and scanning electron microscopy (SEM), with results reported for both A and B counting rules. Gravimetric sampling was also done. Data shown in Tables 13 through 15 include length of operation, length of operation TWA and 8-hr. TWAs. All sample results are blank corrected; fiber counts include fibers rinsed from the cowls.

Note in Table 13 that mean TWAs are consistently below 1 f/cc, except for loose wool installers and feeders working with non-binder wools. For reference, task lengths were reported as: batt installation -

average 3.6 hours/house with 1.2 houses per day; blown installation - average 46 minutes/house, 3.3 houses/day. Airborne fiber geometric mean dimensions were: glass batt - 0.9 Fm x 22 Fm; loose glass wool with binder - 2.0 Fm x 40 Fm; loose glass wool, no binder, installer - 0.6 Fm x 14 Fm; and loose glass wool, no binder, feeder - 0.6 Fm x 15 Fm.

Table 13. Fibrous glass installation exposures, by work group, for task length

	PCM					SEM			
Group*	No. Samples	NIOSH Rules	Mean, f/cc	Range, f/cc	Task TWA	No. Samples	NIOSH Rules	Mean, f/cc	Range, f/cc
FG	24	A	0.23	0.02-0.52	0.20	18	A	0.21	0.05-0.68
		B	0.14	0.02-0.41	0.14	25	B	0.12	0.05-0.41
FGB Ins	29	A	0.85	0.18-3.10	0.84	10	A	0.60	0.17-1.08
		B	0.55	0.17-2.88	0.52	32	B	0.35	0.11-1.14
FGB Fdr	24	A	0.26	0.06-1.01	0.25	8	A	0.17	0.03-0.63
		B	0.18	0.06-0.67	0.l8	15	B	0.13	0.03-0.38
FGNB Ins	21	A	8.13	1.49-20.7	7.70	3	A	6.11	2.53-8.19
		B	7.67	1.32-18.4	7.09	35	B	12.7	0.22-37.0
FGNB Fdr	11	A	1.62	0.06-7.72	1.50	5	A	2.75	1.05-4.92
		B	1.74	0.06-9.36	1.49	27	B	2.06	0.07-9.44

* Abbreviations: FG - fibrous glass batt installer
FGB Ins - loose wool with binder, installer
FGB Fdr - loose wool with binder, feeder
FGNB Ins - loose wool without binder, installer
FGNB Fdr -loose wool without binder, feeder

Table 14. Fibrous glass installation exposures, by work group, for gravimetric task length and 8-hr TWA

	Task Length				8 Hr-TWA		
Group	No. Samples	Mean, mg/m³	Range, mg/m³	Overall TWA	No. Samples	Mean, mg/m³	Range, mg/m³
FG	16	3.94	0.06-8.96	4.58	13	2.14	0.01-9.32
FGB Ins	17	11.1	0.35-46.3	8.39	2	1.22	1.09-1.35
FGB Fdr	24	2.75	0.05-12.3	2.69	6	0.75	0.23-1.30
FGNB Ins	16	12.2	0.43-46.5	10.9	1	1.68	--

FGNB Fdr	27	2.49	0.18-16.9	2.89	4	1.42	0.46-2.44

Table 15. Fibrous glass installation exposures, by work group, for 8-hr TWA

	PCM				SEM			
Group	No. Samples	NIOSH Rules	Mean, f/cc	Range, f/cc	No. Samples	NIOSH Rules	Mean, f/cc	Range, f/cc
FG	19	A	0.09	0.01-0.23	15	A	0.1	0.01-0.37
		B	0.06	0.01-0.17	21	B	0.07	0.01-0.22
FGB Ins	8	A	0.25	0.01-0.66	3	A	0.14	0.02-0.26
		B	0.15	0.01-0.35	9	B	0.08	0.01-0.14
FGB Fdr	7	A	0.07	0.01-0.15	3	A	0.03	0.01-0.06
		B	0.05	0.01-0.13	5	B	0.03	0.01-0.05
FGNB Ins	4	A	2.07	0.40-3.62	0	--	--	--
		B	1.96	0.40-3.23	4	B	3.16	1.35-4.72
FGNB Fdr	1	A	0.84	--	0	--	--	--
		B	0.85	--	3	B	0.85	0.17-2.16

Rock and Slag Wool

Occupational exposures while blowing mineral wool were measured by Esmen *et al.* (1982). The report did not specify whether the material was rock or slag. Results ranged from 0.50 to 14.8 f/cc, with 48% of the fibers being respirable. The highest exposure was to the installer (blower). Head and Wagg (1980) report exposures as high as 20.9 f/ml during loosefill mineral wool installation.

Installation of rock wool blankets was monitored by Marconi *et al.* (1987) using PCM analysis. Fibers were separated as greater than or less than 3 Fm diameter. Ventilation was provided only through the open doors into the spaces being insulated. Personal samples collected on workers directly involved in installation were 14-120 f/L (0.014-0.12 f/cc) for diameters >3 Fm and 9-410 f/L (0.009-0.41 f/cc) for <3 Fm diameters. Approximately 45% of the total fibers collected were respirable.

The Perrault *et al.* (1992) report included two rock wool operations. Blowing rock wool into attic spaces yielded an area geometric average of 0.32 f/cc, with the bulk material sized at 0.50 Fm x 4.0 Fm. The spray application operation average was 0.15 f/cc, with bulk dimensions 2.0 Fm x 22 Fm.
Personal samples of both blown and looselay rock wool insulation workers were reported by Jaffrey (1990). Result means ranged from 0.08-0.55 f/cc, with the highest exposures during blowing operations. Similarly, TIMA (1990) data from mineral wool insulating and ceiling tile installation operations ranged from

<0.01 to 0.58 f/cc. Head and Wagg (1980) reported exposures for sprayed mineral wool and industrial engine exhaust mineral wool applications at 0.16-2.57 f/cc and 0.02-0.35 f/cc, respectively.

The Lees *et al*. (1993) work discussed under fibrous glass also included three work categories for mineral wool. Results are in Tables 16-18. Airborne fiber dimensions were: wool batts - 1.3 Fm x 37 Fm; wool installers - 1.0 Fm x 30 Fm; and wool feeder - 1.6 Fm x 50 Fm.

Table 16. Mineral wool installation exposures, by work group, for task length

	PCM					SEM			
Group*	No. Samples	NIOSH Rules	Mean, f/cc	Range, f/cc	Task TWA	No. Samples	NIOSH Rules	Mean, f/cc	Range, f/cc
MW	8	A	0.24	0.13-0.55	0.19	0	--	--	--
		B	0.17	0.07-0.39	0.14	10	B	0.17	0.06-0.40
MW Ins	9	A	2.99	0.77-8.02	3.97	0	--	--	--
		B	1.94	0.32-6.16	2.66	12	B	1.31	0.29-3.92
MW Fdr	10	A	0.51	0.09-1.14	0.75	0	--	--	--
		B	0.31	0.09-0.78	0.48	8	B	0.29	0.07-0.52

* Abbreviations: MW - mineral wool batt installer
MW Ins - loose mineral wool installer
MW Fdr - loose mineral wool feeder

Table 17. Mineral wool installation exposures, by work group, for gravimetric task length and 8-hr TWA

	Task Length				8-Hr TWA		
Group	No. Samples	Mean, mg/m³	Range, mg/m³	Overall TWA	No. Samples	Mean, mg/m³	Range, mg/m³
MW	2	2.18	2.11-2.24	2.18	1	1.39	--
MW Ins	5	12.2	3.58-24.5	12.1	2	5.58	1.46-9.71
MW Fdr	7	6.46	2.09-11.9	7.53	4	2.92	1.79-4.40

Table 18. Mineral wool installation exposures, by work group, for 8-hr TWA

	PCM				SEM			
Group	No. Samples	NIOSH Rules	Mean, f/cc	Range, f/cc	No. Samples	NIOSH Rules	Mean, f/cc	Range, f/cc
MW	6	A	0.15	0.10-0.21	0	--	--	--
		B	0.11	0.06-0.15	7	B	0.07	0.05-0.14
MW Ins	5	A	1.46	0.31-3.73	0	--	--	--
		B	0.97	0.13-2.44	5	B	0.66	0.10-1.33
MW Fdr	4	A	0.28	0.12-0.59	0	--	--	--
		B	0.18	0.07-0.40	4	B	0.18	0.08-0.23

Schneider and Smith (1984) compared fiber sizes in old and new MMVF products. Old rock wool was taken from manufacturer's housing insulation sample archives, and new samples were obtained from the production line. Punch samples (about 5 grams with a 21 mm diameter punch) were weighed, then vibrated at a known frequency and amplitude. Airborne material and settled dust were sampled during each test chamber run, with all sampling done in duplicate. They found that older products generated more airborne fibers for the same weight of material, and they had a higher ratio of fiber concentration to weight of settled dust. New and old products had essentially the same fiber size distributions, with slightly longer and thinner fibers seen in the older product.

Refractory Ceramic Fibers

Friar and Phillips (1989) reported air sample results for pipe and wrapping insulation, furnace stripping and relining, and blanket handling. Results ranged from 0.6 f/cc when machining ceramic fireboard to 1.75 f/cc during kiln operations. Furnace and kiln lining operations were also evaluated by Head and Wagg (1980), who reported respirable sample results of 0.09-5.64 f/ml.

Gantner (1986) assessed cristobalite during removal of RCF insulation from industrial furnaces. Bulk samples of the after-service material showed that 3-21% was cristobalite. Gantner also determined that 4-14.7% of the total particulate generated during actual removal operations was cristobalite.

Exposures during installation and removal in 13 different furnaces were evaluated by Cheng *et al*. (1992). Sampling was grouped by task, including inspection, minor repair, blanket and module removal and installation and waste handling. By design, sampling was done during the highest expected exposure period rather than for the length of operation, with times from 15 to 375 minutes. For 128 samples, results ranged

from 0.003-17 f/cc, with fiber sizes of 0.5-6 Fm diameter and 5-220 Fm long. The report also included cristobalite results - 0.03 to 0.2 mg/m³ - with sampling done during the expected worse-case furnace lining removal operations.

Cheng *et al*. (1992) included specialized operation sampling as a corollary to the main study. Results are 8-hour TWAs unless otherwise noted: (1) job site heat treating and stress relief - 0.005-0.14 f/cc; (2) removing and disposing of damaged flange and valve insulation covers -area results <0.020 f/cc; personal samples 0.023 and 0.09 f/cc; (3) removing fire damaged RCF - 0.45 f/cc; (4) heat treating furnace loading, unloading and cleaning operation - 0.5 f/cc; short-term sample (22 minutes) during cleaning only - 1.3 f/cc.

General area samples for industrial furnace removal and replacement were reported at 0.39 to 3.51 f/cc, geometric average. The bulk material fibers were sized using TEM at 1.1 Fm diameter and 17 Fm long (Perrault *et al*., 1992).

TIMA (1990) compiled data from 103 end users. Analysis of the data as a whole showed that mean RCF exposures were 1.17 f/cc. Approximately 90% of the samples were <3 f/cc, with 98% of the samples showing exposures <6.2 f/cc.

Large-scale RCF removal and renewal operations in a refinery were monitored by van den Bergen *et al*. (1994). During removal (using pneumatic drilling hammers), personal 8-hr. TWAs were 9-50 f/cc for RCF, 9-54 mg/m³ respirable dust and 0.14-0.81 mg/m³ for quartz. RCF samples were not taken during new lining installation (pneumatic sprayers), but respirable dust results were 3-25 mg/m³, with quartz at 0.05-0.38 mg/m³.

Carborundum Company Fibers Division (1991, 1992a) reported sampling results from cutting, sanding and drilling operations on RCF board to compare results between hand and power and wet versus dry operations. As expected, more dust was generated when using power tools on dry fiber board. Results are in Tables 19-21.

Table 19. Total dust (in grams) from sawing Fiberfrax® Duraboard

Operation	Total dust, (g)
Hand saw with kerf (tooth blade offset)	0.0416
Hand saw without kerf	0.0435
Power jigsaw with kerf	0.2172
Power jigsaw without kerf	0.2257

Table 20. Total dust (in grams) from sanding Fiberfrax® Duraboard

Operation	Total dust (g)
Hand sanding, dry	0.0223
Hand sanding, wet	0.0025
Power sanding, dry	0.2142
Power sanding, wet	0.0256

Table 21. Total dust (in grams) from drilling Fiberfrax® Duraboard

Operation	Total dust (g)
Electric drill with twist bit	0.0707
Cork bore (core drill) - cores removed at site	0.0294
Cork bore - cores removed in disposal bag	0.0099

Carborundum Company Fibers Division (1992b, 1993) sampled simulated furnace lining tamping - the step during which new linings are compressed to ensure a tight, uniform fit. Tamping is also known for causing the highest exposures during installation. Two RCF module sections, one dry and one wet, were placed in closed chambers and tamped 20 times each with a wood block and mallet. Chamber air was sampled for generated dust during the tamping period plus 2 minutes. Results (Table 22) show that less dust is generated when the modules are wetted before tamping, but that adding surfactants to the water or increasing the module saturation does not significantly impact the amount of dust produced.

Table 22. Dust generated during simulated RCF module tamping

Module Treatment	Wetting Coverage	Total Dust (g)	% Dust Reduction
No wetting	----	0.0407	----
Water only	0.5 gal/100 ft²	0.0043	89.4
Water only	1.0 gal/100 ft²	0.0022	94.6
Water only	1.7 gal/100 ft²	0.0023	94.3
Water plus surfactant	0.5 gal/100 ft²	0.0041	89.9
Water plus surfactant	1.0 gal/100 ft²	0.0033	91.9

The tamping experiment was repeated using the 1.0 gallon per 100 ft^2 surface area application rate, with the chamber sampled for fiber generation. Results were: dry tamping - 2.1 f/cc; water only - 0.57 f/cc; and water plus surfactant - 0.55 f/cc. Again, adding a surfactant is of little benefit.

Other Exposures

Historical information on MMVF manufacturing reveals that exposures to other compounds have been common, particularly before the early 1970s. Asbestos gloves and thermal insulations were used in production plants long before the associated health hazards were publicized. Asbestos was often included in the fiber mixtures, especially when the product was going to be used for cement (Enterline *et al*., 1981; Cherrie and Dodgson, 1986; Simonato *et al*., 1987).

Early exposure to polycyclic aromatic hydrocarbons (PAH) in furnace areas is also probable since ventilation was poor. Exposures to arsenic in copper slag plants (Cherrie and Dodgson, 1986) and to coal tars, quartz and other substances have been identified but not quantified (Saracci *et al*., 1984).

Other contaminant exposures in modern manufacturing plants were measured in several studies (Enterline *et al*., 1983; Enterline and Marsh, 1984; Enterline *et al*., 1987). Sampling was sporadic, however, and not representative of long term exposures. Some examples of potential toxic contaminants in typical MMVF manufacturing are: arsenic - 0.01-0.48 Fg/m^3; benzene soluble organics - 0.012-0.52 mg/m^3; respirable silica - 0.004-0.71 mg/m^3; formaldehyde - 0.03-20 ppm; and respirable cristobalite - 0.1-0.25 mg/m^3.

TOXICOLOGICAL DATA REVIEW

For over 40 years, researchers have attempted to determine if exposures to the MMVF will cause adverse health effects in humans. The question became one of public attention after Stanton and Wrench (1972) reported mesothelioma induction in rats after exposure to fibrous glass. Experimental work intensified almost overnight.

The answer is still not definitive. Overall, experimental results show MMVF to be much less pathogenic than asbestos. However, epidemiological and animal studies indicate that MMVF are fibrogenic and cause non-malignant respiratory diseases (NMRD). There is also animal evidence to support classifying fine glass, glass wool and ceramic fibers as possible carcinogens.

One dilemma facing the scientific community is that the epidemiological evidence seems to be moving towards a less clear association between MMVF and mortality or tumor incidence as workers from the very early production years are lost to the cohorts. The ability of the MMVF to produce fibrosis, sarcomas, adenocarcinomas, and other tumors is obvious from the results of numerous animal experiments. However, the vast majority of the animals exhibiting biological activity have been artificially exposed - by injection or implantation of fibers. When inhalation exposure is used, the vitreous fibers' ability to elicit a carcinogenic response is largely negative.

To complicate matters, researchers disagree on the validity of using animal models to mimic human response patterns, For example, particles sized to induce disease in humans may not actually reach rodent target organs (Oberdorster and Lehnert, 1991). Rats are often used for MMVF research, yet have been shown to have a low sensitivity for mesothelioma induction via inhalation (Pott *et al*., 1991). Conversely, hamsters may have heightened sensitivity to mesotheliomas with inorganic and aluminosilicate fibers (Vu and Dearfield, 1993).

A review of the experimental evidence will help explain why so much uncertainty still exists about the MMVF. The studies will be presented by category - *in vitro*, epidemiological and animal. Because the literature is so extensive, the latter two topics are further grouped by fiber type.

IN VITRO STUDIES

In vitro studies have been used mainly to assess the genotoxic and cytotoxic potential of man-made vitreous fibers at the cellular level. Be aware that the correlation between *in vitro* and *in vivo* results has not been well established (Wheeler, 1990). *In vitro* systems lack the complex interaction of normal metabolic processes that occur when a living organism is tested.

Genotoxic experiments on the vitreous fibers are limited. Chamberlain and Tarmy (1977) found that glass fibers (mean size 0.12 Fm x 1.9 Fm) do not appear to induce gene mutations in bacterial cell lines. Another study reported that JM (Johns Manville) Code 100 glass fibers caused chromosomal aberrations and transformations in Chinese hamster cell lines, but the effects were much less severe than those induced by asbestos (Sincock *et al.,* 1982). The dusts were not active in human fibroblast or lymphoblastoid cell lines. No aberrations were observed when JM Code 110 glass was tested.

Fine glass wool (average diameter 0.1-0.2 Fm) caused a significant increase in chromosomal changes in hamster embryo cells. Some glass-treated cells were aneuploid and some tetraploid; cells also showed nuclear size and morphological aberrations. Larger diameter fibers (0.8 Fm) were much less active (Oshimura *et al.*, 1984).

Casey (1983) studied the mutagenic potential of various concentrations of asbestos and fine and coarse glass in several test systems (0.001, 0.01 and 0.05 mg/ml suspensions in Chinese hamster ovary-K1 cells, human fibroblasts and human lymphoblasts). The experiments evaluated both sister chromatid exchange (SCE) assays and cell kinetic rates. Overall, there were no significant differences in SCE between exposed and unexposed cell cultures, but the author noted mitotic delays in all exposed cells (chrysotile > fine glass > crocidolite > coarse glass).

Varying sizes of fibrous glass were tested in Chinese hamster lung (CHL) cells for chromosomal aberrations and in human red blood cells for toxicity (indicated by hemolysis). A total of 35 different materials were evaluated, including 16 asbestos samples, clay minerals, calcium silicates and sepiolite. Glass samples, all made by Johns Manville, were: Code 100 (nominal diameter 0.29-0.32 Fm); Code 104 (nominal diameter 0.39-0.53 Fm); Code 108A (nominal diameter 0.69-1.1Fm); and Code 108B (nominal diameter 1.2-2.3 Fm). Glass lengths were typically 90% less than (<) 5 Fm and 95% <10 Fm. Results are summarized in Table 23. The authors concluded that overall cytotoxicity and biological effects decrease as fiber diameter increases (Koshi *et al.*, 1991).

Tilkes and Beck (1980, 1983) looked at cytotoxicity and fiber dimensions by measuring leucine dehydrogenase (LDH) and beta glucuronidase as indicators for changes in plasma and lysosomal plasma membrane permeability. The study was done on both rat and guinea pig lung macrophages exposed to fibrous glass. They concluded that cytotoxicity was clearly dependent on the fiber's length and diameter. Whereas short fibers were only toxic when they were <0.03 Fm in diameter, long and thin glass fibers were as cytotoxic as chrysotile and crocidolite.

Luoto *et al.* (1997) compared cytotoxicity of glass wool, rock and slag wools and RCF using LDH release in rat alveolar macrophages, sheep red cell hemolysis and reactive oxygen metabolite (ROM) production in human polymorphonuclear leukocytes. The fibers were obtained from the TIMA repository, so are consistent with fiber numbers that will be discussed later in the animal studies. Results showed that RCFs 1 through 3 increased production of ROM, RCFs 1 and 3 showed hemolytic activity and RCF 3 had a small LDH increase. Rock (MMVF 21) and slag (MMVF 22) increased ROM production and

LDH release. MMVF 10, a glass wool, showed significant increase in hemolysis. All results were reported as compared with known reactive (quartz) and non-reactive (titanium dioxide or chrysotile for ROM) controls. Overall, the study suggested that cellular toxicity for these MMVFs is relatively mild.

Table 23. In vitro cell toxicity and chromosomal aberrations for varying diameter fibrous glass

	Cytotoxicity	Hemolysis	% Chromosomal Aberrations	
Material Tested	TD_{50} (Fg/ml)	HD_{50} (Fg/ml)	Abnormalities	Polyploids
Code 100 glass	10	800	2-3	16-32
Code 104 glass	11	>1000	not given	not given
Code 108A glass	18	>1000	2-4	4-18
Code 108B glass	27	>1000	not given	not given
Chrysotile	0.2-3.7	<200	10-19	34-50
Crocidolite	7	>1000	6-12	24-32
Amosite	4.5	>1000	2-6	18-42
Calcium silicates	8-50	210->1000	0-4	4-20

TD_{50} (Toxic $dose_{50}$) - the amount of dust needed to inhibit colony forming efficiency of CHL cells by 50%
HD_{50} (Hemolytic $dose_{50}$) - the dose needed to cause 50% hemolysis in human erythrocytes
Fg/ml - micrograms per milliliter
% Chromosomal aberrations - Fiber doses for these studies were 5, 10, 30 and 100 Fg/ml. Results for abnormalities and polyploidy reflect the range for all doses. "Abnormalities" covers structural aberrations, including gaps, chromosome and chromatid breaks, dicentrics, chromatid exchanges, etc.

Using hamster embryo cells, Hesterberg and Barrett (1984) also found that cell transformations were dependent on fiber dimensions. When glass fiber lengths were held constant and diameters varied, the thinner fibers (average 0.13 Fm) were 20 times more toxic than fibers with diameters in the 0.8 Fm range. When diameters were kept constant and length varied, cell transformations decreased ten fold as the length decreased from 9.5 to 1.7 Fm. No cytological changes were noted when fibers were less than about 1 Fm long.

The ability of long, thin glass fibers to induce cell transformations has been documented by others (Brown *et al*., 1979a, 1979b; Chamberlain *et al*., 1979; Pickrell *et al*., 1983). The cytotoxicity of these particular fibers appears to parallel that found with asbestos.

Rock and slag wool have both been shown to be cytotoxic, but in all cases were much less so than asbestos (Brown *et al*., 1979b; Davies, 1980; Gormley *et al*., 1985; Brown *et al*., 1986).

The limited data for ceramic fibers shows that they cause cytological changes in alveolar macrophages and A549 human type-II cells , but are not toxic to lung fibroblasts (Gormley *et al*., 1985; Brown *et al.*, 1986). In addition, Wheeler and Garner (1988) reported that Fiberfrax® ceramic fibers were less toxic to alveolar macrophages than were chrysotile, crocidolite or amosite asbestos.

Reactive oxygen metabolite production (e.g., hyroxyl radicals, OH^-) has previously been found to be indicative of toxicity for asbestos and some other mineral fibers. Leanderson and Tagesson (1992) evaluated radical formation in natural (chrysotile, amosite, crocidolite, erionite, anthophyllite) and synthetic (rock wool, glass wool and ceramic) fibers. They monitored hydrogen peroxide (H_2O_2) and OH^- produced after mixing fibers with polymorphonuclear leukocytes. All fibers produced radicals, but the natural ones to a much greater degree.

A study by Maples and Johnson (1992) used the same natural fibers (except wollastonite), JM Code 100 glass and glass wool in a non-cellular system. They evaluated the fibers' ability to produce OH^- when incubated with H_2O_2 and salicylic acid at 37E centigrade (C). Although they established a positive correlation between the natural fibers' OH^- production and mesothelioma induction/tumor formation in rats using pleural inoculation, there was no correlation for the man-made fibers. The study suggests further development of this system as a possible *in vitro* toxicity indicator.

Mossman and Sesko (1990) compared fibrous (crocidolite, chrysotile, erionite, JM 100 fibrous glass, sepiolite) and non-fibrous (riebeckite, antigorite, glass beads, mordenite) materials for their ability to induce cellular changes. They monitored: (1) superoxide release from alveolar macrophages (indicator of inflammatory response); (2) ^{51}chromium release from hamster tracheal epithelial cells (predictor for membranolytic potential); and (3) collagen production in rat lung fibroblasts (fibrogenic potential). Dose related increases in superoxide concentrations were seen with crocidolite, JM 100 and erionite. Similarly, crocidolite, JM 100 and chrysotile caused increased rates of chromium release. Collagen protein production increased with the asbestos fibers only. Apparently, fibrous materials are more likely to adversely affect cellular metabolism than are chemically similar non-fibrous analogs.

Leanderson and Tagesson (1989) tested *in vitro* exposures to glass wool, rock wool, and ceramic fibers for possible synergistic effects with cigarette smoke. Calf thymus was exposed to the smoke alone, individual fibers alone and to combinations. Deoxyribonucleic acid (DNA) damage was assessed by following hydroxylation of deoxyguanosine (dG). The idea was that DNA-damaging OH^- are generated from the hydrogen peroxide in cigarette smoke. If OH^- generation is catalyzed by MMVF, there should be significant increases in hydroxylation of dG when combination exposures occurred versus exposures of any of the materials alone.

A significant increase in hydroxylation was indeed found, but only from the rock wool/cigarette smoke combination. Leanderson and Tagesson theorized that the rock wool combination reaction resulted from its high iron content. The iron interacted with the hydrogen peroxide in the smoke to enhance its disso-

ciation to free radicals, which were then readily available for hydroxylation of the deoxyguanosine. Apparently, MMVF were not acting as catalysts in the reaction.

Fibers from the TIMA fiber repository were tested in chinese hamster ovary (CHO) cells by Hart *et al.* (1994) to determine effects on cell proliferation, viability and nuclear abnormalities. Test fibers include Manville 475 glass, Manville 901 glass, refractory ceramic fibers, glass, rock and slag wool, experimental vitreous fiber, crocidolite and chrysotile. For all fibers tested, there were concentration-dependent decreases in cell proliferation and increases in the incidence of nuclear abnormality. Based on the concentration of fibers per square centimeter (f/cm^2) required to reduce cell proliferation to half that of the unexposed controls (EC_{50}), fiber toxicity increases with length up to about 20 Fm. For diameters in the 0.3 to 7 Fm range, cell toxicity differences appear to be independent of diameter (when the fiber concentration is expressed as f/cm^2). The apparent mode of toxicity was actually cytostasis, resulting from fiber ingestion by, or attachment to, the CHO cells. This then interfered with cell division.

The study also assessed the usefulness of the CHO cells as an indicator of toxicity in humans. Though the fibers spanned a wide range of chemical composition, cell toxicity was apparently independent of fiber type when lengths were equivalent. That is, glass, RCF and mineral wool all induced similar cell toxicity. Chrysotile was 5-fold more toxic than crocidolite, when in other systems (e.g., human bronchial epithelial), it is usually 100-fold or more toxic. MMVF animal studies to date show that only RCF induce mesotheliomas. The authors concluded that CHO cells may not be an appropriate *in vitro* test system for fiber toxicity.

EPIDEMIOLOGICAL STUDIES

Though there are only a few epidemiological studies on man-made vitreous fibers, several have involved large cohorts that have been followed for long periods. Current knowledge is derived mainly from three major studies conducted in Europe, the United States and Canada. All of the studies have centered on the incidence of lung cancer, but cancers at other sites have been reported.

The evidence suggests a possible correlation between lung cancer and exposure to rock, slag, and glass wools, but the lack of dose-response relationships makes interpretation difficult (Doll, 1987). Miettinen and Rossiter (1990) also recommend that the epidemiological evidence be tempered with an understanding that the early production processes involved many exposures to substances other than MMVF, such as asbestos and polycyclic aromatic hydrocarbons (PAH), that cannot be separated from the MMVF exposure. In addition, they point out that results may be confused by inconsistent or inadequate cohort and control group selection criteria. Finally, smoking habits and socioeconomic confounders may not be adequately integrated with the epidemiological data over the lifetime of the study. Lee *et al.* (1995) provide a comprehensive look at epidemiological data to date that is worthy of review, including summary tables and discussion.

Davies and Cherry (1992) raise concerns about some assumptions used in epidemiological studies. They initiated a study to determine the types of fibers actually present in airborne samples collected in a continuous glass filament plant. Airborne samples were taken from all phases of the production plant, including quality control, pre-production, laboratory, production line and oven area. Analysis by scanning electron microscopy showed respirable levels of <0.001-0.017 f/ml and total counts <0.001-0.069 f/ml. Using electron microscopy with energy dispersive X-ray spectroscopy to determine the composition of these samples, Davies and Cherry found calcium sulfate, organic fibers, asbestos and glass wool - but no continuous glass. Consequently, epidemiological data generated on workers at this plant might assume - erroneously - that findings were attributable to continuous glass.

European Study

The European study involves a total of 25146 workers at 13 manufacturing plants located in seven European countries. The plants include 7 rock/slag wool, 4 glass wool, and 2 continuous filament manufacturers. Workers were entered on employment, which ranged from 1900 to 1955, and the initial report followed them through 1977 (Saracci *et al.*, 1984). This study reported a two-fold increase in lung cancer mortality for continuous glass workers having over 30 years employment. However, the authors cautioned that there was not a clear correlation between the cancers and fiber exposure, since the standardized mortality ratio (SMR) was not adjusted for cigarette smoking, previous exposures to asbestos or socioeconomic status.

Of the 1505 observed deaths, there was no significant elevation in total deaths or total cancer deaths. There was a trend in rock wool workers for higher SMRs for cancer of the trachea, bronchus and lung as the time since first employment increased. The authors suggested that this increased risk was associated with the work environment conditions that existed 30 years ago. Similar trends were not found in continuous filament or glass wool employees.

Results of a 1981 to 1983 follow-up of the European cohort was reported by Simonato *et al*. (1986). This study included correction factors not used in the earlier study, such as adjustments in the SMR for local and regional mortality rates. In addition, this time the study only looked at exposed personnel rather than all employees, and examined mortality based on period of exposure. Examination of manufacturing history led Simonato *et al*. to divide the cohort into: (1) early production years, when no dust suppression was used and procedures were labor intensive; (2) intermediate technology years, when controls were being implemented, but not uniformly; and (3) late technology, after engineering controls and mechanization were routine.

The new assessment again showed elevated mortality from lung cancers among rock wool and slag wool workers, but only during the early production years. It is known that during this era, ventilation was poor and PAH exposures were common from the furnace fumes. Workers were also exposed to arsenic contaminants in copper slag (Cherrie and Dodgson, 1986; Claude and Frentzel-Beyme, 1986).

Because of the correlation of lung cancers with the early years, Fallentine (1990) attempted to recreate early production methods so that the possible incidental exposures could be evaluated. He found high concentrations of PAH, total dust, and lead (ranging from 4.2-5.1 mg/m^3) in the cupola area. Formaldehyde, phenols and tar distillates were also present.

Simonato *et al.* (1986) reported excess lung cancers in glass wool workers when SMRs were calculated with national mortality rates. When the figures were adjusted for local mortality rates, the SMR was not statistically significant.

Boffetta *et al.* (1992) attempted to use a multivariate model based on Poisson regression to validate previous reports on the European cohort. They analyzed data from the cohort as a whole, and broke out rock/slag and glass wool subpopulations. Looking only at lung cancer deaths (cancer of the trachea, bronchus or lung), they confirmed original study findings that reported excess lung cancer mortality (189 observed, 151.2 expected for rock/slag workers). Time since first employment was the variable most strongly associated with lung cancer risk in the subpopulations.

The European study has noted cancers at other sites, though most are not statistically significant within the cohort. Simonato *et al*. (1987) reported an increase in bladder cancers in rock/slag workers, but could not find a correlation with any particular technological phase. They also found a statistically significant increase in buccal and pharyngeal cancers in the rock and slag wool industry. Bertazzi *et al.* (1984) noted a small excess of cancer of the larynx in the Italian glass wool and filament subcohort. Similarly, Moulin *et al*. (1986) assessed the French subcohort and reported significant increases in the incidence of cancers of the larynx, pharynx and buccal cavity. Comparable findings were not reported by any other countries in the study.

Environmental surveys conducted from 1977-1980 by Ottery *et al*. (1984) at 12 of the European plants showed that the average respirable fiber exposures were <0.1 f/ml for glass, rock, and slag wool and <0.01 f/ml for continuous filament.

It is worthy of note that only one case of mesothelioma has been reported during the European study. The man died after only two years in MMVF production. Based on the knowledge that asbestos mesotheliomas rarely occur less than 20 years after the first exposure, researchers are assuming that this exposure is probably unrelated to vitreous fiber exposure.

United States Study

Bayliss *et al.* (1976) evaluated 1448 workers at a United States fibrous glass plant. The men had at least five years of employment in the industry and were hired between 1940 and 1949. The authors reported a statistically significant increase in deaths from NMRD, excluding influenza and pneumonia. The study did not assess confounders such as smoking or previous occupation history. Available records show that

workers in the cohort were exposed to respirable fibers, median diameter 1.8 Fm, with a mean concentration of 0.08 f/ml (range of 0.01-0.83 f/ml). Follow-ups were not done since this cohort was included in a much larger U.S. study, reported below.

In the United States, 17 production plants have been studied, including 6 glass wool, 3 glass filament, 2 plants producing both glass and filament and 6 rock and slag plants. The original cohort involved 14884 glass workers and 1846 rock/slag production personnel. Workers were employed in production or maintenance for at least one year during the 1945-1963 time period, except for two plants producing small diameter glass fibers (<1.5 Fm), where a minimum six month employment was required.

Preliminary reports followed the cohort through 1977 and concluded that there was no correlation between MMVF production and respiratory cancers. Of 247 respiratory cancer deaths, 236 were lung, 10 laryngeal and 1 mediastinal. There were no mesotheliomas. These studies found a significant excess of NMRD deaths for both the total cohort and for the small diameter glass fiber workers in particular. Disease occurrence could not be correlated with fiber exposures (Enterline *et al.*, 1981; Enterline *et al.*, 1983; Enterline and Marsh, 1984).

Enterline *et al*. (1983) updated the cohort for the period January 1946 through December 1977. This included 16730 male production and maintenance workers employed at least one year in one of the 17 U.S. plants during 1945-1963. They reported excess lung cancer among the cohort during early production of rock and slag, presumably for the same reasons as those cited in the European study. The authors also found significant elevations of non-malignant respiratory disease, but could not attribute the increase to any cumulative fiber exposures.

A five year update (1978-1982) by Enterline *et al*. (1987) extended the study by looking at production of groups of fibers. For fine glass production, they found a significant excess of neoplasms and lung cancers in workers with more than 20 years employment. The correlation trends were less dramatic when the SMR was calculated using local corrections. The update concluded that there was an association between the fibers and increased health risk, but could not identify a definite relationship between respiratory cancer, duration of exposure, and exposure levels. Respiratory cancers for glass wool and filament workers were not significantly elevated, even for those with more than 20 years exposure.

In the mineral wool plants, there was an overall increase in respiratory cancer, but it was independent of exposure level or duration. The nested study, when corrected for smoking, did show a relationship between respiratory cancer and fiber exposure for mineral wool workers, mainly attributable to the slag plants. Enterline (1990a, 1990b) points out, however, that it is "fairly certain" that asbestos was used in at least four of the six U.S. plants studied, and these exposures cannot be separated from the MMVF. The authors also caution that contaminants in the slag cannot be ruled out as contributors to carcinogenicity estimates.

As a note of reference, mean fiber exposures for this update ranged from 0.003-0.021 f/cc for small diameter glass, 0.005-0.29 f/cc in glass wool production and 0.195-0.427 f/cc in the rock and slag plants.

Marsh *et al*. (1990) presented additional 3-year follow-up results for the United States cohort for 1983 to 1985. For the entire study period - 1945 to 1985 - there is a small statistically significant excess of all malignant neoplasms and respiratory cancers, with the greatest respiratory cancer excess found in mineral wool workers (SMR 135.7, $P<0.5$). For the small diameter glass, overall numbers of respiratory cancer were slightly elevated, but the numbers were much lower than those reported by Enterline *et al*. (1987). The update concluded that, overall, there was no cause-and-effect relationship between fiber exposure and respiratory cancer in the cohort. They also failed to find an association between exposure and non-malignant respiratory disease.

This update concludes that there is weaker cumulative evidence for a correlation between lung cancer mortality and MMVF exposures. Marsh *et al*. speculates that as the study continues, the correlation may further decrease as workers from the early production years die and are lost to the cohort. The United States study thus far has reported a total of three mesotheliomas. One of the workers had a possible previous exposure to asbestos; another case lacked complete employment history.

Several reports analyze the statistical significance of the lung cancer SMR reported by Enterline *et al.* (1987) in the U.S. cohort update (Chiazze and Watkins, 1994; Chiazze *et al.*, 1992, 1993, 1995). One Owens-Corning glass plant in Newark, Ohio, accounted for 38% of the glass cohort in the elevated SMR report. Researchers conducted a case-control study of lung cancer and non-malignant respiratory disease at this particular plant. Of 164 possible cases of lung cancers from 1941 to 1982, 144 cases were studied. Airborne exposures were estimated for 1934-1987 using employment history records and reviews, interviews and historical reconstruction of the plant environments. With unadjusted odds ratios, lung cancer was correlated with smoking and with employment year of hire and age of first hire. NMRD was correlated only with smoking. When variables were considered in logistic regression models, only smoking and age at first hire were statistically significant for lung cancer, with smoking again the only significant variable for NMRD. Other exposures that showed increased odds ratios for cancer risk, though not statistically significant, were talc and asphalt fume for lung cancer, and asbestos, silica, respirable fibers and asphalt fume for NMRD.

The authors also had a special interest in whether fine diameter glass fibers increased the risk of lung cancer or NMRD. They identified 44 workers who were at the plant during fine fiber production and analyzed them separately for risk. They found no suggestion that exposure to fine fibers had increased the risk for lung cancer, although the relationship was less clear for NMRD.

Attempting to establish ties between fiber deposition and lung cancer deaths in the U.S. cohort studied by Enterline *et al*. (1987), McDonald *et al*. (1990) obtained lung tissue samples from 145 workers with at least one year of employment at one of the 17 U.S. plants between 1940 and 1963. Each subject was matched with a referent, defined as the next available male autopsy with the same or adjacent year of death

and birth, and whose death was attributed to something other than a malignant disease. Tissue samples were evaluated using phase contrast microscopy for fiber counts, transmission electron microscopy for fiber sizing, energy dispersive spectroscopy for elemental composition and selected area electron diffraction for structure determination. Total fiber counts showed a statistically significant excess in workers vice referents, with MMVF, asbestos and other fibers identified. However, there were no significant excesses of any particular fiber type, and MMVF were seen in very low concentrations (seen in 28 of 112 samples). MMVF have been shown to leach cations and "dissolve" in rat lungs, and the low incidence in the study tissue samples may be attributable to this same action.

Goldsmith and Goldsmith (1993) looked at the United States cohort for non-respiratory disease trends that could be associated with MMVF exposure. They reported an increased incidence of mortality from nephritis and/or nephrosis, suggesting that incidental silica exposures may have contributed to the increased renal disease.

Other Epidemiological Studies - Fibrous Glass, Glass Wool, Rock and Slag Wool

A perspective study by Shannon *et al*. (1987) reviewed glass wool fiber workers in Ontario, Canada. The cohort was 2557 workers employed at least 90 days between 1955 and 1977. Follow-up lasted through 1984. Overall mortality was below expected values, but lung cancer deaths were slightly elevated. The data could not be correlated with either length of exposure or time since the first exposure occurred. In fact, the highest SMR was recorded for those having the shortest exposure times. Actual fiber concentrations, estimated from industrial hygiene data collected since 1978, were "rarely" above 0.2 f/ml.

In a follow-up study, Shannon *et al*. (1990) looked at 1456 workers with at least one year of employment at the Ontario glass plant from 1951 through the end of 1986. Lung cancers were slightly more than expected when compared with the Ontario population (11 cases, 8.1 expected; SMR 136), but overall mortality was less than expected. The authors reported that dust samples in the plant from 1979 to 1987 showed TWAs ranging from 0.02-0.05 f/ml, with the highest recorded value 0.91 f/ml.

Another historical perspective by Spurny *et al*. (1983) looked at 1374 French male glass wool workers employed at least one year. Although no excess lung cancer rates were found, there was an increased incidence of upper respiratory and alimentary tract cancers.

Chest roentgenograms of 1389 employees at a fibrous glass production plant (mainly glass wool) were used to assess pulmonary disease prevalence by Wright (1968). The study group included all employees with at least 10 years employment at the plant, but excluded those who had worked for more than one year in the prefabrication department because of possible exposure to silica in the raw materials. Dust sample results throughout the plant averaged 2.24 mg/m^3 (range 0.93-13.3 mg/m^3), with <1% of the particles sampled determined to be fibrous (85% of particles 2-10 Fm median diameter; 6% <20 Fm length). The

author states that this data was collected during the study and that effective exhaust ventilation controls were in place. Therefore, they serve as maximum exposures for the study population. There was no meaningful difference in findings of disease, shadows or pleural calcifications based on length of exposure for the roentgenograms reviewed.

Utidjian and deTreville (1970) further evaluated this cohort with pulmonary function testing for 232 randomly selected members. There was no correlation between exposure to glass and pulmonary function test (PFT) abnormalities. A cohort subset, consisting of older employees from the highest and lowest expected exposure groups, was given complete physical examinations, PFT and x-rays (Hook *et al*., 1970). They found essentially no differences in overall health between the groups, regardless of exposure.

Nasr *et al*. (1971) evaluated chest X-rays from 1832 fibrous glass workers (about 67% employed over 10 years) and 196 office workers in the same plant. Employees with poor quality films or no known fibrous glass exposure were excluded, so that final study group represented 91% of the work force. Radiographic abnormalities were seen in 16.84% of the office workers and 16.16 % of the production workers. Abnormalities most often noted were increased lung markings, abnormal aorta, abnormal heart and emphysema. Overall, there were no statistical differences in abnormality prevalence between the exposure and control groups.

Similarly, Hill *et al.* (1973) used radiography, questionnaires and spirometry to compare 70 glass workers with known zero exposure controls. The study group, with 12-24 years of exposure (mean 19.85 years), was matched with the control group (warehouse workers) for age, sex, height, weight and geographical location. Environmental air sample results in the plant were: breathing zone, respirable fibers - 1.0-5.5 f/cc; "bench top" height, respirable fibers - 3.4-10.7 f/cc; breathing zone, total dust - 0.4-12.7 mg/m^3; "bench top" height, total dust - 26-185 mg/m^3. There was no evidence for increased respiratory hazards or decreased pulmonary function in the glass workers.

Morgan *et al*. (1981) did a retrospective mortality study of 6536 male fibrous glass workers employed between 1968 and 1977. The cohort was employed at Owens-Corning Fiberglas® Corporation for at least 10 years. No statistically significant excess of deaths was attributable to fibrous glass exposure. The authors also evaluated "long-term" employees, having at least 30 years since first employment. There was no increased mortality for any cause of death for the 1222 workers in the subset.

A cross-sectional morbidity study by Weill *et al.* (1983) assessed data gathered from questionnaires and medical examinations. There were 1028 males from seven United States fibrous glass and rock/slag wool plants in the cohort. This included two plants producing coarse glass (average diameter 3 Fm), two plants making both coarse and fine glass (1-3 Fm), one producing fine glass only (<1 Fm) and two mineral wool plants. Average work experience for the group was 18 years. No evidence was found of respiratory effects in the population, nor was there a discernible correlation between symptomology and fiber exposures. The study did report a relationship between exposure to fine fibrous glass and an increased presence of parenchymal small opacities observed on x-rays.

Hughes *et al*. (1993) reassessed the Weill *et al*. cohort's respiratory health to determine if there were any radiographic changes. The follow-up evaluated 1259 workers from the five glass plants and 185 from the mineral wool plants. Of the original cohort, 64% were still employed, and 87% of these participated in the follow-up. The update reaffirmed a low level of small opacities in workers (23/1435 or 1.6%) when compared with the blue collar comparison population (2/305 or 0.7%). Of the workers with opacities, 21/23 worked at the two plants with the highest documented exposures to fine fibers. Overall, there were no adverse clinical functional or radiographic effects seen in the cohort. There was no significant excess of NMRD found in the mineral wool (slag) production workers.

A study of mortality patterns among rock and slag workers was reported by Robinson *et al.* (1982). The cohort consisted of 596 workers who were followed from their last date of employment (between 1940 and 1948) through 1974. Members of the cohort were categorized by job and by the resultant likelihood of fiber exposure. Collected in 1975, personal TWA samples results were 0.10-1.95 f/cc, with fibers sized at 1.7-2.7 Fm x 6.8-24.8 Fm (median dimensions by PCM). Though there was no correlation between exposure and lung cancer, the authors did report increased deaths from cancer of the digestive system and from NMRD for workers with over 20 years exposure.

In a similar study, Malmberg *et al.* (1984) looked at pulmonary function in rock wool workers with over ten years of exposure. Chest x-rays were normal and lung function tests showed no abnormalities.

Wong *et al*. (1991) conducted a case control study of lung cancer in 4841 male slag wool workers. They were attempting to address other studies that had not fully characterized exposure data, had not shown a dose-response relationship or did not control for cigarette smoking or exposure to other carcinogenic contaminants. To be included, workers had to have at least 1 year of employment at one of the 9 slag plants studied (4 of these plants were also in the U.S. epidemiological cohort study). Two plants were known to have used arsenic contaminated copper slag, 4 plants had used asbestos and one plant had used refractory ceramic fibers. Cases were defined as lung cancer deaths from 1970 through the end of 1989, with controls selected randomly from deaths by other causes, and matched for age, race and the plant where they worked. Exposure data, gathered from industrial hygiene surveys, showed an airborne concentration of 0-0.25 f/cc.

There were a total of 504 deaths during the study period, with 55 of the 61 lung cancers included in the analysis (unable to get control matches or locate families for 6 cases). Wong *et al*. found no statistically significant difference between cases and controls for exposure duration, and no apparent association between exposure duration and lung cancer risk, both with and without adjustments for smoking history. They did find a dose-response relationship between pack-years of cigarette smoking and lung cancer risk, but could not correlate risk with exposure to MMVF. The authors acknowledge that the study had limited airborne fiber exposure data and that some information was subject to error since it was obtained second-hand from family members.

Engholm *et al*. (1987) followed approximately 135000 Swedish construction workers exposed to both MMVF and asbestos. The workers were examined regularly from 1971 to 1974, and follow-ups continued through 1982 for incidence of cancer and mortality. Overall, the study showed excess occurrence of pleural mesotheliomas, but it was not significantly higher in those exposed to MMVF when compared with non-exposed controls. The authors note their inability to separate the MMVF and asbestos exposure effects.

Workers known to have minimal or no exposure to other stressors often encountered in the insulating industry (e.g., asbestos, arsenic, furnace fumes) were followed by Gustavsson *et al*. (1992) to evaluate mortality and cancer rates. The cohort consisted of 2807 male workers employed at least one year at various Swedish prefabricated housing plants. Of these, 1068 had documented exposures to MMVF. The study followed mortality from 1969-1988 and cancer incidence from 1969-1985. There were 14 lung cancer deaths in the cohort (20.7 expected based on regional rates), with 2 lung cancer cases after a 20-year latency period (4.3 expected). Exposure ranges for various work categories were determined by estimating historical data (0.20-0.25 f/ml) and by sampling current conditions (0.02-0.17 f/ml). Wood dust exposures, also considered significant for this group, were reported at 0.09-1.9 mg/m^3 (respirable dust 8-hr TWA). Gustavsson *et al*. found no total or cause-specific mortality correlated with the time since first employment, and no correlation between lung cancer mortality and level of exposure or length of employment. They suggest further follow-up since their study captured a relatively short latency period for the cohort.

Other Epidemiological Studies - Refractory Ceramic Fibers

Epidemiological information on refractory ceramic fibers is mostly limited to work done by the Thermal Insulation Manufacturers Association (TIMA) and more recently, the Refractory Ceramic Fiber Coalition (RCFC). In 1987, TIMA initiated a five year respiratory medical surveillance study at the University of Cincinnati to follow 617 RCF workers at 6 United States plants. Standardized surveillance included lung function testing, x-rays and physical examinations. Carborundum Company started a concurrent epidemiological study which expanded the cohort to include former employees, added work and medical histories, additional x-ray views and included tissue examination upon a cohort member's death. The two studies eventually merged, and the resultant study extended beyond the initial five years.

The 1989 interim respiratory analysis showed "pleural abnormalities" in 1.9% of the workers (TIMA, 1990). By 1992, preliminary results of the combined studies, now having a cohort of almost 900, showed: no evidence of fibrotic lung disease on x-ray; a slight but statistically significant downward trend in lung function results associated with length of exposure, though this finding was judged not to be clinically significant; pleural plaques in 3.5% of the workers, correlated with duration of exposure and time since first MMVF exposure; and no excess cancer mortalities (Carborundum Company, 1991).

The 1994 update reported an increased number of employees with respiratory symptoms such as coughing, wheezing and shortness of breath. There appeared to be a correlation between symptoms and length of exposure, but researchers warn that similar patterns of respiratory symptoms and distributions are seen in studies of dusty work environments. Lung function test results were shown to be dependent on smoking habits - RCF workers who smoked showed greater decreases in lung function measurements than would be expected from smokers with no RCF exposure. Pleural plaques were reported in 0.9% (11/117) of workers with less than 10 years RCF exposure, 2.8% (7/248) of those with 10-20 years exposure and 12.5% (9/72) having more than 20 years exposure. The cohort remains free of lung fibrosis, with no excess lung cancers or mesotheliomas reported (Carborundum Company, 1992, 1994a, 1994b).

LeMasters et al. (1994) reported a correlation between pleural changes and RCF exposures. They found pleural changes in 6/29 workers with more than 20 years in the RCF production industry, and 8/70 workers with more than 20 years since first exposure.

These results were not confirmed in a study commissioned by the European Ceramic Fiber Industry Association (ECFIA). Trethowan *et al*. (1995) conducted a cross-sectional morbidity survey of 628 RCF employees in 7 European manufacturing plants. The study evaluated all full-time employees, mean age 37.7 years, through self-administered health questionnaires, lung function testing and chest x-rays. Overall, 44% of participants smoked and 19% had worked in dusty occupations prior to RCF plant employment. The authors found: (1) common reports of nasal stuffiness, eye irritation and skin irritation; (2) no correlation between chronic bronchitis and cumulative respirable fiber exposure; (3) small opacities in 13% of participants were not correlated with fiber exposure; and (4) no chest x-ray abnormalities that were related to fiber exposures.

Industrial hygiene surveys and air samples for the ECFIA study were reported by Burge *et al.* (1995). Fibers were counted using the WHO/EURO reference method (phase contrast microscopy, respirable fibers defined as < 3Fm diameter, >5 Fm long and >3:1 aspect ratio). Inspirable mass measurements, defined as that portion of particulate material likely to enter the nose or mouth, were collected using preweighed filters in an inspirable dust sampling head. Inspirable dust sample means were 1.7-3.4 mg/m^3 for primary production and 1.8-11.2 mg/m^3 for secondary production processes. Respirable fiber sample result means were 0.2-0.88 f/ml for primary and 0.49-1.36 f/ml in secondary production.

Correlating the health exposure information with the health analyses, Trethowan *et al*. (1995) found that the high incidence of upper respiratory, eye and skin irritation was correlated with both the respirable and inspirable dust levels. Decreases in lung function were related to increasing cumulative exposures to respirable fibers, but only for smokers and ex-smokers.

ANIMAL TOXICITY STUDIES

The majority of evidence on the health risks associated with MMVF exposure comes from animal studies. These can be divided into those that introduce the fiber through inhalation - the method thought to most closely model human exposure - and those that artificially introduce the fiber by injection or implantation. For simplicity, each route of exposure is discussed individually for each fiber group.

To simplify the complex and extensive information - details of fiber sizings, aerosol and injection mixtures, animal ages and longevity, histological and cytological findings, experimental procedures and so on - the data is presented either in tables or as summaries of the final animal responses. Information on fiber sizes, length or amount of exposure and experimental shortcomings are provided as needed for clarity. Consult the individual references for complete details of the studies.

MMVF animal data and its use are not without controversy. Opinions are divided on whether the available data are sufficient to classify glass wools as probable carcinogens as published in the Seventh Annual Report on Carcinogens (NTP, 1994). Based on their review of glass studies from 1976 through 1993, Infante *et al.* (1994) concluded that the evidence supports the NTP listing. They champion injection and implantation studies as the primary means of evaluating human risk, stating that inhalation studies do not deliver sufficient fiber doses to the lungs to mimic human disease response.

Others argue that inhalation studies are the best means of assessing human risk. They contend that inhalation studies to date do not support glass carcinogenicity (Hesterberg *et al*., 1993; Bunn *et al*., 1993a, 1993b; McClellan, 1994) . Brown *et al.* (1991) concurs by saying that evidence exists only for the carcinogenicity of special purpose glass, and then only when it is injected directly into the pleural or peritoneal cavity.

Another point of contention is whether intratracheal and intraperitoneal protocols adequately predict inhalation reactions. Several reports conclude that tumors can result in intratracheal and intraperitoneal tests simply because of the large doses introduced (Eastes and Hadley, 1994; Johnson, 1994; Eastes *et al*., 1995). For example, even fibers found to have relatively quick dissolution rates will cause tumors when injected in sufficiently high doses. This may also be attributed to the fact that following injection, some fibers come out of suspension as bundles or clumps, rather than remaining individual fibers. This changes not only the fiber distribution (dose delivered) to the target organ, but also affects the body's reaction to the material. On the other hand, when fibers are inhaled, they remain "single." As verified by fiber dissolution rate and retention studies, many fibers quickly dissolve, thereby decreasing fiber resident time (contact time). If inhaled fibers contact lung fluids, only the most durable fibers would be expected to cause tumors. Implantation and injection protocols bypass these effects.

Collier *et al.* (1994) found that fibers were more durable in the peritoneal cavity than the lung, possibly indicating that the peritoneum is more sensitive to tumor induction. Further, when increasing amounts of fibrous material were injected intraperitoneally into rats, material above about 1.5 mg was found in nodule-like clumps, either free in the cavity or loosely attached to peritoneal organs. These clumps elicited inflammatory reactions typical of those seen with any foreign body.

There are also disagreements over whether rats or hamsters are the study animal of choice for MMVF inhalation research. Based on intrapleural injection studies with glass and RCF, Rutten *et al*. (1994) contends that there are species-specific response differences that may well be critical to development of and mechanisms for fiber-induced pleural diseases.

Another issue under discussion concerns lung burden and fiber counts reported in animal studies. For example, Warheit *et al.* (1991) evaluated methods for lung tissue digestion to recover retained fibers in lung tissue after. They incubated a variety of fibers in saline (negative control, pH 7.2), bleach (5.25% hypochlorite, pH 10.6) and potassium hydroxide (11% KOH in ethanol and water, pH >14) to determine if fiber sizes might be affected simply by the digestion technique itself. Fibers tested included crocidolite, chrysotile, kevlar, wollastonite, polyacrylonitrile (PAN)-based carbon and glass. All were verified by SEM as $5 Fm long and having an aspect ratio >3:1. All fiber dimensions were affected by incubation in the bleach and KOH digestion systems when compared with the negative control. For glass, mean length decreased and mean diameter increased in KOH.

A follow-up study was done to investigate the unexpected diameter increases in some of the fibers. The authors guessed that the thinnest fibers could be dissolving completely, thereby indirectly increasing the mean diameter counts. Fibers were treated as before in bleach and KOH, but the solution was filtered and fibers counted with PCM. Results for glass fibers were 18.7 f/mm^2 for saline, compared with 17.9 f/mm^2 for bleach and 11.4 f/mm^2 in KOH, showing that the bleach and KOH may have dissolved some smaller fibers. Based on these results, the study cautions researchers to evaluate effects of digestion techniques before reporting fiber clearance rates.

Using the inhalation data produced during the Research and Consulting Company (RCC) studies on RCF, Yu *et al.* (1994) developed mathematical models of fiber clearance from rat lungs. Previous work showed that fiber clearance rates were dependent on fiber size, especially the length, and that clearance rates tended to be slowed down when the fiber burden was high. The RCC information led to the following general conclusions: (1) rat lung clearance rates are higher for RCF than for those of non-fibrous particulates; (2) there is no apparent fiber size that is cleared preferentially; (3) and RCF clearance rates decrease with increasing lung burden. Based on these trends, the authors point out that high exposure dosing during inhalation studies could result in false positive tumor induction results. That is, if tumor induction is actually a function of fiber dose and residence time, then high dosing leads to slower clearance, causing longer fiber retention and increasing the likelihood of adverse lung effects. Further, Yu *et al*. states that the rat's dose response function may be nonlinear (may be convex curve). This would mean that past data interpretation, which assumed a linear relationship, may be flawed and/or inappropriate.

Johnson (1994) provides a good overview of many of the controversial issues presented here. Keep these issues in mind as you read and evaluate the following information.

Fibrous Glass

Intratracheal Instillation

Intratracheal instillation introduces a large bolus of material directly into the trachea. The dose may be administered as a single large injection or as several smaller injections over a period of time. Overall, results of these studies for fibrous glass range from macrophage aggregation and mild fibrotic responses to lung tumors.

Pott *et al.* (1987) did weekly instillation on rats over a 20 week period using glass wool fibers (median size 0.18 Fm x 3.2 Fm). Crocidolite was the positive control and saline was used for the negative control. Five of 34 animals receiving the glass fibers developed lung tumors. The controls produced 15 tumors in 35 (15/35) crocidolite animals and 0/40 saline controls. A conflicting result was found by Smith *et al.* (1987). They injected rats with five weekly doses of 2 milligrams (mg) of glass wool fibers (median diameter 0.45 Fm, length 4.7 Fm). Two of the crocidolite controls developed broncho-alveolar tumors and 24/25 had significant fibrosis. All other test animals were negative for tumors; 7/22 had fibrosis. Note that the number of test animals, 22, was very small.

Two groups of larger glass fibers (sized at 1.5 Fm x 5 Fm and 1.5 Fm x 60 Fm) were injected in rats by Drew *et al.* (1987) in 10 weekly doses of 0.5 mg (total dose 5 mg). Although macrophage aggregation and granulomatous foreign body response were observed, there were no fibrotic effects or tumors in test animals. Fibrosis was noted in crocidolite controls.

A hamster study by Pott *et al.* (1984a) showed that very thin glass fibers of JM Code 104 produced lung cancers and mesotheliomas in hamsters. Animals were given 8 weekly instillations of 1 mg glass dust per dose. The challenge dust was either <0.3 Fm x <4.2 Fm or <0.3 Fm x <7 Fm. Surprisingly, the animals getting glass developed more mesotheliomas than did the crocidolite hamsters, with the longer fibers inducing more tumors than short fibers. Actual tumor rates were: test animals short fibers - 38/138; test animals long fibers - 48/136; crocidolite - 18/142. However, most of the animals lived 18 months after instillation, and 50% lived longer than two years.

Adachi *et al.* (1991, 1992) instilled female Syrian hamsters weekly with 2.0 mg fibrous glass (mean 0.65 Fm diameter x 16.8 Fm length) for five weeks. Animals were observed for 24 months, then sacrificed. There were 2/20 tumors for glass (1 squamous cell carcinoma in lung; 1 neuroblastoma in adrenal gland), with 0/20 negative controls (no injection), 2/20 amosite asbestos (1 mesothelioma, 1 lung adenoma) and 0/20 crocidolite controls. Slight lung inflammation and pleural thickening were observed in test animals.

Household insulation products of varying diameters, as well as glass microfibers (<0.2 Fm median diameter) and crocidolite were tested in hamsters (Pickrell *et al.*, 1983). Most of the animals receiving glass microfibers were dead within 30 days of instillation. This was attributed to the injection procedure

and not to biological activity. No tumors were observed in the other glass test animals, although inflammation and fibrotic lesions were seen.

Renne *et al.* (1985) documented alveolar septal fibrosis in hamsters that were given varying amounts of Tempstran Code 100/475 glass fibers weekly for 15 weeks. Fiber median diameter was 0.75 Fm, with median length 4.3 Fm. Results were: total dose 0.75 mg (15 injections of 0.05 mg each) - 7/26 test animals had fibrosis; total dose 7.5 mg (at 0.5 mg each) - 15/25; total dose 15 mg (at 1.0 mg each) - 10/25; and total dose 150 mg (at 10.0 mg each) - 24/25. Negative controls (saline) had a fibrosis rate of 7/27, with cage controls 2/25. Animals instilled with quartz exhibited fibrosis at the following rates: 9/25 (total dose 0.45 mg), 11/27 (total dose 4.95 mg), 19/26 (total dose 49.5 mg) and 17/25 (total dose 90 mg).

A similar study looked at fine fibrous glass reactions in guinea pigs. All fibers were sized at 0.1-1.0 Fm diameter. Fibers used in the single 4 mg dose were 92% >10 Fm long, while fibers in the 25 mg dose were 93% <10 Fm in length. Fibrotic lesions were found only with the longer glass, but were fewer in number than those observed in crocidolite animals (Wright and Kuschner, 1977).

Intrapleural Administration

An ongoing debate about animal toxicity studies, particularly for MMVF, is that fiber kinetics, dissolution rates and deposition/retention is not adequately characterized. Bermudez (1994) developed a model to quantitate fiber recovery in rats after intrapleural instillation, but notes that fiber translocation mechanisms must be understood before this method can be applied successfully in inhalation studies. Bermudez instilled male Fischer rats with varying doses of known glass fibers (10^3, 10^4, 10^5, 10^6 f/cc doses of TIMA MMVF 10; mean dimensions 1.31 ± 0.85 Fm diameter and 22.25 ± 18.64 Fm long), fluorescent microspheres (used as controls; 10^6/ml dose; mean diameter 2.3Fm) or saline (negative controls). Thirty minutes after instillation, liquified agarose gel was added to the pleural cavity and allowed to set. The gel casts were recovered, reliquified and centrifuged, with the resultant pellet resuspended and counted using PCOM (test animals) or green filter (controls). The results showed mean recovery rates of 90.3% microspheres and 72-94% over the dose range for fibers. No fibers were seen in the negative control animals. The most variable recovery was seen in the animals dosed at 10^6 f/cc, attributed to the difficulty in delivering a dense suspension.

Wagner *et al.* (1973) delivered single intrapleural injections of fibrous glass (maximum diameter 7 Fm, 60% >20 Fm long), glass powder and chrysotile asbestos into rats. There were no tumors in the glass fiber group, 1 mesothelioma in the glass powder animals, and tumors in 44/68 asbestos controls.

Monchaux *et al.* (1981) injected rats intrapleurally with a single 20 mg dose of fine fibrous glass (JM Code 104). Mean fiber size, determined by transmission electron microscopy, was 0.229 Fm diameter x 5.89 Fm long. There were mesotheliomas in 6/45 of the test animals, 14/33 for chrysotile controls, 21/39 in

crocidolite controls and 0/32 in saline control animals. There was also 1 carcinoma in the chrysotile controls. The authors noted that an outbreak of pneumonia in the test animal house about 400 days post-injection could have masked some carcinoma occurrence.

In another study of varying glass dimensions, rats were given a single dose of either 20 mg of fine glass wool (99% <0.5 Fm diameter, median length 1.7 Fm) or coarse glass wool (17% <1 Fm diameter, median length 22 Fm). Four of the 32 rats exposed to fine fibers developed mesothelioma; no tumors were induced by the coarse fiber group. All saline controls were negative (0/32) (Wagner *et al*., 1976).

Wagner *et al*. (1984) looked at glass wool again, but this time they injected rats with a 20 mg dose of JM Code 100 glass microfiber and English glass wool dusts - most #1 Fm diameter and #5 Fm long. No tumors were found in the negative controls. Mesotheliomas developed in 4/48 JM Code 100 animals, 1/48 glass wool and 6/48 chrysotile animals.

Stanton and Wrench (1972) and Stanton *et al*. (1977, 1981) did single dose implantation in rats using resin coated fibrous glass, uncoated glass and asbestos (40 mg in gelatin carrier on pledget). The animals were followed for two years. Pleural mesotheliomas were observed in the glass test group from a low of 0 in 28 animals to a high of 20 in 29 animals. Also reported was the finding that fibers less than 1.5 Fm in diameter and greater than 8 Fm long were the most likely to elicit fibrotic responses and were most likely to be carcinogenic. This assessment was modified in later years to state that, as long as the fiber length was maintained, much smaller diameter fibers were most likely to produce cancers (McConnell *et al*., 1984; Pott *et al*., 1984b). Control animal mesothelioma rates were 17/615 for the pledget alone and 3/491 for untreated animals.

Intraperitoneal Injection

Most of the intraperitoneal studies on glass wool have been done by Pott *et al*. (1976, 1984b, 1987, 1990, 1991). They found that fine glass fibers and glass wools produced mesotheliomas (also sarcomas and carcinomas) and there appeared to be a dose-response relationship. Study results are summarized in Table 24.

Smith *et al*. (1987) injected hamsters and rats with a single 25 mg dose of glass wool (19% of fibers 0.2-0.6 Fm diameter x >10 Fm long). In rats, mesotheliomas were found in 8/25 animals treated with glass and in 20/25 injected with crocidolite. Hamster crocidolite controls had tumors in 8/25, but test animals developed no tumors. There were no tumors reported for any untreated or saline control animals. Fibrosis was noted in 76% of the test rats, 60% crocidolite controls and 0% saline and cage controls.

Inhalation

Rats were exposed to glass fiber dust clouds (mean dimensions 0.51 Fm diameter x 5.5 Fm long) by Nambu *et al*. (1992). Exposure was for 6 hours/day, 5 days/week for 4 weeks, with average fiber concentrations of 10.8 ± 3.3 mg/m^3. Test animals were sacrificed at 24 hours, 1 week, 6 months and 1 year post-exposure, and lung tissues examined. Respirable sized glass fibers were seen in lung tissues and animals had slight pulmonary inflammation.

Additional fibrous glass inhalation studies are summarized in Table 25. Most data are for glass wool, though continuous filament and superthin (micro) fibers are also included.

Table 24. Fibrous glass intraperitoneal injection studies by Pott *et al.* (abbreviations are defined at end of table)

Experimental Animal	Exposure Schedule	Exposure Dose	Fiber Dimensions	Challenge Material	Results**	Reference Notes
Wistar rats	single dose	2 mg	50% <0.4 Fm d x 59% <3 Fm l	glass wool	1/34	Pott *et al.* (1976)
	"	10 mg	"	glass wool	4/36	
	25 mg/w, 4 w	100 mg	"	glass wool	23/32	Authors state results support a dose - response relationship between fine glass and mesothelioma.
	single dose	2 mg	---	chrysotile	6/37	
	"	25 mg	---	chrysotile	25/31	
	single dose	10 mg	---	granular dust	3/263	
				negative control (saline)	0/72	
	single dose	2 mg	0.2 Fm d x 10 Fm l (means)	glass wool	20/73	
	"	10 mg	"	glass wool	41/77	
	2- 25 mg doses	50 mg	"	glass wool	55/77	
	single dose	2 mg	---	crocidolite	15/39	
	single dose	50 mg	granular	corundum (aluminum oxide)	3/37	
Wistar rats	single dose	2 mg	50% < 0.33 Fm d x 2.4 Fm l	JM 100 glass microfibers	2/44	Pott *et al.* (1984b)
	"	2 mg	50% < 0.24 Fm d x 1.4 Fm l	JM 100 glass microfibers	2/44	
	single dose	10 mg	50% < 0.39 Fm d x 2.7 Fm l	JM 104	4/45	Results reflect sarcomas or mesotheliomas.
	single dose	10 mg	50% < 0.29 Fm d x 4.8 Fm l	JM 104, milled 1 hr.	27/37	
	"	2 mg	"	JM 104, milled 2 hr.	14/44	
	"	10 mg	"	JM 104, milled 2 hr.	29/44	
	"	10 mg	"	JM 104, milled 4 hr.	19/39	
	single dose	0.4 mg	50% < 0.11Fm d x 0.9 Fm l	chrysotile	9/44	
	"	2 mg	---	chrysotile	26/44	
	"	10 mg	---	chrysotile	35/44	
	single dose	10 mg	50% < 0.22 Fm d x 1.2 Fm l	crocidolite	15/43	
	single dose	2 mg	granular	corundum (aluminum oxide)	1/45	
	"	90 mg	granular	corundum	0/118	
	single dose	5 mg	granular	negative control (titanium	0/50	
	"	90 mg	granular	dioxide)	0/118	
				negative control (titanium dioxide)		

Experimental Animal	Exposure Schedule	Exposure Dose	Fiber Dimensions	Challenge Material	Results**	Reference Notes
Sprague-Dawley rats (15 month results)	single dose	2 mg	50% < 0.33 Fm d x 2.4 Fm l	JM 100 glass microfibers	1/54	
	"	10 mg	"	JM 100 glass microfibers	1/54	
	single dose	2 mg	50% < 0.32 Fm d x 4.4 Fm l	JM 100 glass, 20 minute cutting	3/54	
	"	2 mg	50% < 0.32 Fm d x 4.1 Fm l	JM 100 glass, 40 minute cutting	5/54	
	single dose	5 mg	50% < 0.29 Fm d x 4.8 Fm l	JM 100 glass, milled 1 hr.	22/54	
Wistar rats	single dose (Exp 11)	5 mg	50% <0.29 Fm d x 4.8 Fm l	JM 104 glass wool cut & mill ground 1 hr.	20/45	Pott *et al.* (1987)
Experiments 7, 11	single dose (Exp 7)	10 mg	50% <0.3 Fm d x 3.5 Fm l	JM 104 glass wool	13/26 (&)	Results reflect sarcoma, carcinoma or mesothelioma of the abdominal cavity
	"	10 mg	"	cut & mill ground 2 hr.	18/33 (%)	
	single dose (Exp 11)	5 mg	50% <0.5 Fm d x 5.3 Fm l	JM 104 glass wool, treated 24 hr. with 1.4 N HCl	2/45	
	single dose (Exp 11)	5 mg	50% <0.5 Fm d x 5.4 Fm l	JM 104 glass wool, treated 24 hr. with 1.4 N NaOH	27/46	
	single dose (Exp 11)	5 mg	granular	negative control (titanium dioxide)	0/47	
Experiment 13	single dose	0.5 mg	50% <0.18 Fm d x 3.2 Fm l	JM 104/475 glass fibers	5/30	Note that controls were not used in each experiment.
	"	2 mg	"	cut & mill ground 30 minutes	8/31	
	single dose	2 mg	---	JM 104/475 glass fibers, treated 24 hr. with 1.4N HCL	16/32	
	single dose	1 mg	50% <0.11 Fm d x 0.9 Fm l	chrysotile UICC/B	27/32	
	single dose	0.5 mg	50% <0.03 Fm d x 1.2 Fm l	chrysotile (Calidria)	2/32	
	single dose	0.5 mg	50% <0.20 Fm d x 2.1 Fm l	crocidolite	18/32	
	"	2 mg	"	crocidolite	28/32	
	3 doses (2+4+4)	10 mg	granular	negative control (titanium dioxide)	0/32	
	single dose	1 ml		negative control (saline)	2/32	
Experiment 15	5-1 mg doses	5 mg	50% <0.18 Fm d x 3.2 Fm l	JM 104/475 glass fibers cut & mill ground 30 minutes	35/53	
	single dose	0.05 mg	50% <0.11 Fm d x 0.9 Fm l	chrysotile UICC/B	7/36	
	"	0.25 mg	"	chrysotile UICC/B	21/34	
	"	1 mg	"	chrysotile UICC/B	31/36	
	5-20 mg doses	100 mg	granular	negative control (titanium dioxide)	5/53	
	5-2 ml doses	10 ml		negative control (NaCl solution)	2/102	

Experimental Animal	Exposure Schedule	Exposure Dose	Fiber Dimensions	Challenge Material	Results**	Reference Notes
Experiment 6	single dose single dose single dose single dose	10 mg 10 mg 10 mg 10 mg	50% <0.47 Fm d x 2.2 Fm l 50% <0.02 Fm d x 0.2 Fm l granular granular	JM 106 glass chrysotile UICC/A milled negative control (aluminum oxide) quartz	2/39 1/39 3/35 2/34	
Experiment 5	single dose " single dose	50 mg 250 mg 4 ml	50% <3.7 Fm d x 16.5Fm l "	ES3 glass filament ES3 glass filament negative control (saline)	3/48 4/46 2/45	
Experiments 2, 4	single dose (Exp 2) 2-20 mg doses (Exp 2) single dose (Exp 4) 2-20 mg doses (Exp 2)	10 mg 40 mg 250 mg 40 mg	50% <5.5 Fm d x 39 Fm l " " granular	ES5 glass filament ES5 glass filament ES5 glass filament quartz	2/50 5/46 2/28 9/41	Pott *et al.* (1987), continued
Experiment 2	2-20 mg doses	40 mg	50% <7.4 Fm d x 46 Fm l	ES7 glass filament	1/47	
Experiments 2, 5	2-20 mg doses (Exp 2) single dose (Exp 5) " single dose (Exp 5)	40 mg 50 mg 250 mg 4 ml	--- --- --- 	granular glass (ground to fine dust) granular glass granular glass negative control (saline)	2/45 4/48 4/48 2/45	
Experiment 1	single dose " single dose single dose	6 mg 25 mg 6 mg 	50% <0.15 Fm d x 9 Fm l " --- 	Chrysotile UICC/A Chrysotile UICC/A Chrysotile UICC/A, HCl treated negative control (saline)	26/34 25/31 0/38 0/70	
Sprague-Dawley rats Experiment 10	single dose single dose single dose single dose single dose single dose	5 mg 5 mg 5 mg 5 mg 5 mg 5 mg	50% <0.29 Fm d x 4.8 Fm l " 50% <0.5 Fm d x 5.3 Fm l --- 50% <0.5 Fm d x 5.4 Fm l granular	JM 104 glass wool cut & mill ground 1 hr. JM 104 glass wool, treated 2 hr. with 1.4 N HCl JM 104 glass wool, treated 24 hr. with 1.4 N HCl JM 104 glass wool, treated 2 hr. with 1.4 N NaOH JM 104 glass wool, treated 24 hr. with 1.4 N NaOH negative control (titanium dioxide)	44/54 32/54 4/54 42/54 46/53 2/52	

Experimental Animal	Exposure Schedule	Exposure Dose	Fiber Dimensions	Challenge Material	Results**	Reference Notes
Experiment 12	single dose " single dose 2- 2 ml doses	2 mg 10 mg 2 mg 4 ml	50% <0.33 Fm d x 2.4 Fm l " 50% <0.32 Fm d x 4.4 Fm l ---	JM 100 glass fibers (dust) JM 100 glass fibers (dust) JM 100 glass fibers, cut & ground 20 minutes negative control (NaCl solution)	21/54 24/53 26/54 3/54	
Wistar rats	1 mg/w, 5 w single dose " " single dose " " 20 mg/w, 5 w 5 ml/w, 2 w	5 mg 0.05 mg 0.25 mg 1.00 mg 0.01 mg 0.05 mg 0.25 mg 100 mg 10 ml	50% <0.15 Fm d x 2.6 Fm l 50% <0.05 Fm d x 0.67Fm l " " 50% <0.1 Fm d x 1.10 Fm l " " ---	JM 104/475 glass fibers chrysotile chrysotile chrysotile actinolite actinolite actinolite negative control (titanium dioxide) negative control (saline)	34/53 12/36 23/34 30/36 8/35 15/36 20/36 2/53 2/102	Pott *et al*. (1989) Results reflect sarcoma or mesothelioma in the abdominal cavity.
Wistar rats	20 mg/w, 3 w single dose 20 mg/w, 3 w single dose 20 mg/w, 3 w single dose single dose single dose single dose	60 mg 20 mg 60 mg 20 mg 60 mg 6.7 mg 20 mg 6.7 mg 20 mg 6.7 mg 20 mg 6.7 mg 20 mg 2 mg 20 mg	1.06 Fm d x 7.4 Fm l 1.68 Fm d x 10.7 Fm l " 1.40 Fm d x 17.8 Fm l " 0.49Fm d x 4.2 Fm l " 0.51Fm d x 6.0 Fm l " 0.37Fm d x 3.3 Fm l " 0.34 Fm d x 5.6 Fm l " 0.14 Fm d x 2.3 Fm l granular	B-1K (Bayer AG glass type 3101) B-1M B-1M B-1L B-1L B-2K (Bayer AG glass type 3101) B-2L B-2L B-3K (Bayer AG glass type 3102) B-3L B-3L M-475 (JM 104) negative control (titanium oxide)	3/46 1/48 1/46 1/48 5/46 0/48 0/46 0/45 2/44 10/48 30/47 19/48 31/47 8/48 0/47	Pott *et al*. (1990, 1991) [Information on fiber durability and sizing reported by Bellman *et al*. (1990) and Muhle *et al*. (1991).] Results reflect sarcoma or mesothelioma in the abdominal cavity.

Experimental Animal	Exposure Schedule	Exposure Dose	Fiber Dimensions	Challenge Material	Results**	Reference Notes
Wistar rats	50 mg/w, 3 w	150 mg	1.06 Fm d x 7.4 Fm l	B-1K (Bayer AG glass type 3101)	1/32 (48)	Pott *et al*. (1991)
	50 mg/w, 2 w	100 mg	1.19 Fm d x 11.0 Fm l	B-1ML (Bayer AG glass type 3101)	1/39 (48)	Parenthetical numbers are original # rats
	50 mg/w, 2 w 2 ml, 5 w	100 mg 10 ml	0.51 Fm d x 6.0 Fm l	B-2L (Bayer AG glass type 3101) negative control (NaCl solution)	1/35 (48) 2/50 (72)	(undiagnosed lung disease in months 12 & 13 killed some animals).

** Results are given as number of tumors/number of test animals

Exposure schedule: Exp = experiment mg - milligrams
ml - milliliters w - weeks

Fiber dimensions: d - diameter
l - length

Table 25. Fibrous glass and glass wool animal inhalation studies (abbreviations are defined at end of table)

Experimental Animal	Exposure Schedule	Exposure Dose	Fiber Dimensions	Challenge Material	Results, # Tumors/# Test Animals (Tumor Type)	Reference Notes
Rat, hamster	6 h/d, 5 d/w, 24 m	135 mg/m³	0.5 Fm average d; >10 Fm l	glass with binder uncoated glass negative control	no tumors	Gross *et al*. (1970) Authors note small number animals and poor overall survival rate.
Hamster	not specified	25 mg	0.1 Fm d; 80% >20 Fm l 0.33 Fm d; 46% >20 Fm l 1.23 Fm d; 34% >20 Fm l 0.9 Fm d; 0-2% >20 Fm l 0.41 Fm d; 0-2% >20 Fm l 1.49 Fm d; 0-2% >20 Fm l	fibrous glass	9/60 2/60 2/60 0/60 0/60 0/60	Smith *et al*. (1980) Tumor types not reported
Sprague-Dawley rat Guinea pig Hamster	6 h/d, 5 d/w, 90 d with 21 m follow-up 6 h/d, 5 d/w, 90 d with 21 m follow-up 6 h/d, 5 d/w, 90 d with 21 m follow-up	700 f/cc 3100 f/cc 700 f/cc 3100 f/cc 700 f/cc 3100 f/cc	24% < 3 Fm d; >5 Fm l 38% < 3 Fm d; >5 Fm l 24% < 3 Fm d; >5 Fm l 38% < 3 Fm d; >5 Fm l 24% < 3 Fm d; >5 Fm l 38% < 3 Fm d; >5 Fm l	fibrous glass amosite negative control (unexposed) fibrous glass amosite negative control fibrous glass amosite negative control	0/11 (P), 2/11 (BA) 3/11 (2 BA, 1 E) 0/13 2/7 (BA) 0/5 0/5 0/9 0/5 0/7	Lee *et al.* (1981) Note extremely small number of test animals and the short duration of exposure.
Baboon	7 h/d, 5 d/w, 35-40 m	5.8 mg/m³ 13.45 mg/m³	70% <1 Fm d; 60% < 6.3 Fm l 20% >0.5 Fm d; 25% >3Fm l	glass fibers crocidolite	0/10 (marked fibrosis) 0/10	Goldstein *et al.* (1983, 1984)

Experimental Animal	Exposure Schedule	Exposure Dose	Fiber Dimensions	Challenge Material	Results, # Tumors/# Test Animals (Tumor Type)	Reference Notes
Wistar rat	5 h/d, 5 d/w, 50% for 12 m, 50% for 24 m	5 mg/m³	SG glass wool - 69% <1 Fm d; 42% <10 Fm l JM 100 glass - 43% <0.1 Fm d; 94% <5 Fm d NOTE: Dimensions given are for total fibers.	SG glass wool JM Code 100 chrysotile negative control (unexposed)	1/45 (P) 0/48 9/47 (P) 0/47	Le Bouffant *et al.* (1984, 1987)
Fischer 344 rat	7 h/d, 5 d/w, 12 m with 12 m follow-up	10 mg/m³	0.3-2 Fm d 0.3-2 Fm d	JM Code 100 chrysotile negative control	0/55 11/56 (4 A, 7 AC) 3/53 (AC)	McConnell *et al*. (1984)
Fischer 344 rat	7 h/d, 5d/w, 12 m with 12 m follow-up	10 mg/m³	52% < 1 Fm d; 72% 5-20 Fm l 47% < 1 Fm d; 58% 5-20 Fm l 97% < 1 Fm d; 93% 5-20 Fm l 29% < 0.5 Fm d; 37% >10 Fm l	coated glass wool uncoated glass wool JM Code 100 chrysotile negative control	1/48 (AC) 1/47 (AC) 1/48 (AC) 12/48 (11 AC, 1 A) 0/48	Wagner *et al.* (1984)
Fischer 344 rats	7 h/d, 5 d/w, 21 m	15 mg/m³ 5 mg/m³	4-6 Fm d; >20 Fm l 0.5-3.5 Fm d; >10 Fm l <3.5 Fm d; >10 Fm l <3.5 Fm d; >10 Fm l	coated glass wool coated glass wool uncoated glass wool uncoated glass wool	0/100 0/100 0/100 0/100 0/100	Mitchell *et al*. (1986)
Monkey	7 h/d, 5 d/w, 18 m	15 mg/m³ 5 mg/m³	4-6 Fm d; >20 Fm l 0.5-3.5 Fm d; >10 Fm l <3.5 Fm d; >10 Fm l <3.5 Fm d; >10 Fm l	negative control coated glass wool coated glass wool uncoated glass wool uncoated glass wool	no tumors, no fibrosis in any test animals	

Experimental Animal	Exposure Schedule	Exposure Dose	Fiber Dimensions	Challenge Material	Results, # Tumors Test Animals (Tu Type)
Wistar rat	12-24 m	5 mg/m³	69% < 1 Fm d; 42% < 10 Fm l 43% < 0.1 Fm d; 97% <5 Fm l	glass wool JM Code 100 glass chrysotile air control	1/45 (P) 0/48 9/47 (P) 0/47
Wistar rat (nose only inhalation)	5 h/d, 4 d/w, 12 m	3 mg/m³ 2.2 mg/m³ 6 mg/m³	90% <0.8 Fm d; 90% <12.4 Fm l 90% <0.46 Fm d; 90% <4.5 Fm l 90% <1.6 Fm d; 50% <6 Fm l	JM Code 104 crocidolite chrysotile negative control cage control	1/107 (SCC) 1/50 (AC) 0/50 0/55 0/50
Syrian golden hamster	6 h/d, 5d/w, 24 m with lifetime follow-up	0.3 mg/m³ 3 mg/m³ 10 mg/m³ 1.2 mg/m³ 12 mg/m³ 9 mg/m³ 7 mg/m³	0.4 Fm d; 4.9 Fm l " 1.2 Fm d; 24 Fm l 1.1 Fm d; 20 Fm l " 3.0 Fm d; 83 Fm l 97% <5 Fm l	JM Code 100 " CT blowing wool JM building insula-tion (binder) OC wool (binder) Crocidolite Negative control Cage control	0/70 0/69 overall, 0- 0/60 animals ha 0/65 fibrosis 0/66 0/61 0/58 (24% fibrosis 1/58 (BA) (7% fib 0/112 (3% fibrosis
Osborne-Mendel rat	6 h/d, 5d/w, 24 m with lifetime follow-up	0.3 mg/m³ 3 mg/m³ 10 mg/m³ 1.2 mg/m³ 12 mg/m³ 9 mg/m³ 7 mg/m³	0.4 Fm d; 4.9 Fm l " 1.2 Fm d; 24 Fm l 1.1 Fm d; 20 Fm l " 3.0 Fm d; 83 Fm l 97% <5 Fm l NOTE: Fiber dimensions are geometric means.	JM Code 100 " CT blowing wool JM building insula-tion (binder) OC wool (binder) Crocidolite Negative control Cage control	0/57 0/57 overall, 5- 0/52 animals ha 0/61 fibrosis 0/57 0/58 3/57 (2 BA, 1 M) fibrosis) 0/59 (10% fibrosis 0/125 (14% fibros
Fischer 344 rat	7 h/d, 5d/w, 21 m	5 mg/m³ 5 mg/m³ 15 mg/m³ 15 mg/m³	91.1% < 3.5 Fm d; <10 Fm l 96.5% < 3.5 Fm d; >10 Fm l 99.4% < 3.5 Fm d; >10 Fm l 97.1% >3.5 Fm d; >20 Fm l	MT 100/475 MT 100/475 OC FM series (binder) FG insulation glass (binder)	No tumors in 500 rats
Cynomolgus monkey	7 h/d, 5d/w, 18 m	Same as rats	Same as rats	Same as rats negative control (filtered air)	No tumors in 60 t monkeys

Experimental Animal	Exposure Schedule	Exposure Dose	Fiber Dimensions	Challenge Material	Results, # Tumors Test Animals (Tu Type)
Fischer 344 rat	6 h/d, 5d/w, 24 m with follow-up till 20% survival	3 mg/m³ 16 mg/m³ 30 mg/m³	1.26 Fm d x 13.1 Fm l	glass wool (MMVF 10 [JM 901])	0/117 1/118 (A) 7/119 (6A, 1C)
	aerosolized, nose-only inhalation, with fiber equivalents of: 3 mg/m³ . 30 f/ml 16 mg/m³ . 150 f/ml 30 mg/m³ . 240 f/ml	3 mg/m³ 16 mg/m³ 30 mg/m³	0.69 Fm d x 13.7Fm l	glass wool (MMVF 11 [CT B])	4/118 (3A, 1 C) 9/120 (6A, 3 C) 3/112 (3A)
		10 mg/m³	0.08 Fm d x 1.2 Fm l NOTE: Dimensions are geometric means of aerosol fibers.	chrysotile (see Notes) negative control (filtered air)	13/69(7A, 6C, 1 M 4/123 (3A, 1C)

Exposure schedule: h - hours
d - days
w - weeks
m - month

Fiber dimensions: d - diameter
l - length

Challenge material: C - Carborundum
CT - Certainteed
JM Code 100 - Johns Manville microfiber glass
JM Code 104 - Johns Manville fine glass wool
JM 901 - Johns Manville fine glass wool
MT100/475- Manville Tempstran Code 100/475 glass
OC-Owens-Corning
SG - Saint-Gobain (French wool)

Tumor type: A - adenoma
AC - adenocarcinoma
B - bronchial carcinoma
BA - broncho-alveolar adenoma
E - epidermoid carcinoma
M - mesothelioma
P - unspecified pulmonary tumor
SCC - squamous cell carcinoma

Following the negative findings in the Hesterberg *et al.* (1993) rat chronic inhalation studies, Hesterberg and Hart (1994) evaluated the relevancy of such inhalation studies for human risk assessments. They reviewed exposure data from glass manufacturing, installation and removal studies, requiring that analysis was done using the NIOSH 7400 method (primarily B rules) to be included in the comparison. This resulted in 1569 manufacturing samples, 273 end-user (installers) samples and 12 from removal operations. The highest human exposure was recorded during loose wool installation, with an 8-hour TWA average of 1.96 f/cc (mean task length average 7.67 f/cc). Human exposure averages, in f/cc, were: manufacturing glass wool - 0.065; installing batt fiberglass - 0.09; removing ceiling and pipe insulation - 0.04. For comparison, outdoor samples averaged 0.0007 f/cc and indoor ambient samples taken before batt installation and <24 hours after batt installation were 0.00005 and 0.0002, respectively.

In the animal studies, the highest exposure dose reported is 30 mg/m^3, equivalent to about 232 f/cc for MMVF 10 and 246 f/cc for MMVF 11. Rat challenge aerosols were comparable to human exposures with regard to fiber sizes and fiber retention in the lung (fibers/mg dry lung), but were much higher than any documented human exposures. However, the inhalation studies yielded no treatment-induced lung fibrosis, no mesotheliomas and no statistically significant increase in lung tumor incidence in the test rats.

Rock and Slag Wool

Intratracheal Instillation

Adachi *et al.* (1991, 1992) instilled female Syrian hamsters with 2.0 mg rock wool (mean 6.1 Fm diameter x 296 Fm length) weekly for five weeks. After 24 months, there were no tumors observed in 20 test animals or in the 20 negative controls (no injection). Positive controls were 0/20 crocidolite and 2/20 amosite. Slight lung inflammation, pleural thickening and fibrosis were reported in test animals.

Intrapleural Administration

The Stanton *et al.* (1977, 1981) intraperitoneal implantation studies on fibrous glass also included a single slag wool sample. After 24 months, one pleural sarcoma developed in 25 test rats. Negative controls developed 3 mesotheliomas (491 animals).

Single injections of 25 mg of wool in rats (48 animals in each test group) produced 3 mesotheliomas with rock wool fibers with binder and 2 mesotheliomas in the non-binder rock wool group. There were 6 mesotheliomas in asbestos control rats and no tumors in slag wool-treated animals. Most of the injected fibers were <0.6 Fm long (Wagner *et al.*, 1984).

Intraperitoneal Injection

Pott *et al*. (1984b, 1987) tested mineral wools intraperitoneally. In one experiment, rats received two 40 mg doses of slag wool, either fine (median diameter 1.5 Fm, length 14 Fm) or coarse (median diameter 2.6 Fm, length 26 Fm). Test animals developed sarcomas and mesotheliomas (2/96 fine; 6/99 coarse). No tumors occurred in the negative control group.

When rats were injected with 75 mg of rock wool (median diameter 0.64-1.9 Fm, length 4.1-23 Fm), there was a high incidence of sarcoma, mesothelioma and carcinoma in the coarse fiber test animals. Fine fibers also produced tumors, but at a much lower rate. The authors note that the rock wool used was an experimental fiber that was not available for commercial purchase.

Pott *et al.* (1991) included a single slag fiber sample in an extensive study on various mineral fibers and dusts. Wistar rats were given five weekly injections of 30 mg slag (fiber size 1.21 Fm x 9.0 Fm). There were 2/28 tumors (mesothelioma or sarcoma of abdominal cavity) in test animals, with 2/50 in negative controls. In months 12 and 13 of the experiment, some animals were killed by an unidentified infection (the original number of slag animals was 36; original negative controls 72).

A long term particulate study of various man-made and naturally occurring fibers by the Bologna Institute of Oncology included 4 samples of rock wool. In a study update, Maltoni and Monardi (1989) report final results for the wool samples. Sprague-Dawley rats were given a single intraperitoneal injection of the test fibers (25 mg in 1 ml water) and observed for 104 weeks. With an average latency time of about 80 weeks, 3/40 rats had peritoneal mesotheliomas. Untreated UICC chrysotile controls had tumors at the rate of 30/40 for a 25 mg dose (average latency 76 weeks). There were 0/40 tumors in negative control (water) animals.

Inhalation

Though limited, the rock and slag wool inhalation studies are mostly negative. Rats exposed to 5 mg/m^3 of respirable rock wool (23% <1 Fm diameter; 57% <10 Fm long) for 5 hours per day, 5 days per week for both 12 and 24 months had no tumors (0/47). Tumors developed in 9/47 chrysotile test animals (LeBouffant *et al*., 1984, 1987). A similar study exposed rats to 10 mg/m^3 of rock wool for 12 months (7 hours/day, 5 days/week; 1 Fm diameter x 8 Fm long). Adenomas were seen in 2/48 test rats, with tumors in 12/48 controls (Wagner *et al.*, 1984).

Exposure to slag wool was assessed in both rats and hamsters using nose-only inhalation of 7.8 mg/m^3 dust clouds with a mean fiber size of 0.9 Fm diameter and 22 Fm long. Exposure was 6 hours per day, 5 days per week for 2 years. Tumors were observed in 0/55 test rats and 0/69 test hamsters. Crocidolite control animals, exposed for 1 day, 30 days and 24 months gave the following results: rats - tumors were seen in 1/59, 1/61 and 3/57, respectively; hamsters - 0/47, 0/64 and 0/58, respectively (Smith *et al*., 1987).

In October 1990, the Research and Consulting Company MMVF study began testing mineral wool. For slag, exposure scenarios were the same as those used for glass and RCF. Rats were exposed nose-only to 3, 16 or 30 mg/m^3 (27 f/ml, 123 f/ml or 210 f/ml, respectively) of slag wool fibers at the rate of 6 hours/day, 5 days/week for 12 months. Average fiber size was 1 Fm diameter and 20 Fm long. Animals were sacrificed periodically for histological examination, then held for 24 months. Crocidolite control animals showed fibrosis at 3 months, while exposure animals showed minimal pulmonary changes at all exposure levels, with minimal progression noted. No lung changes were observed in air controls. Pulmonary neoplasms were found as follows: 2/116 (1 adenoma, 1 carcinoma) at 3 mg/m^3; 0/115 at 16 mg/m^3; 3/115 (2 adenomas, 1 carcinoma) at 30 mg/m^3; 15/106 (10 adenomas, 5 carcinomas [with 2 mesotheliomas]) in crocidolite controls; and 2/126 (2 adenomas) in the negative controls.

.

Rock wool exposures were similar, except that fiber equivalents to the 3, 16 and 30 mg/m^3 were 34, 145 and 247 f/ml, respectively. No pulmonary changes were reported for air controls, chrysotile controls exhibited fibrosis at 3 months, and the 16 and 30 mg/m^3 test animals showed fibrosis at 18 months, though the authors note that a few of the 30 mg/m^3 animals showed fibrosis at 6 months. Test animal results for 3, 16 and 30 mg/m^3 were 5/114 (4 adenomas, 1 carcinoma), 5/115 (4 adenomas, 1 carcinoma) and 5/114 (4 adenomas, 1 carcinoma), respectively, with positive and negative controls the same as those in the slag results above (Bunn *et al*., 1993a; McConnell *et al*., 1994).

Refractory Ceramic Fibers

Intratracheal Instillation

Intratracheal instillation results were obtained during the Smith *et al*. (1987) studies. Hamsters and rats were instilled weekly with 2 mg RCF (83% >10 Fm long, 86% <2 Fm diameter) for 5 weeks (total dose 10 mg). No tumors were observed in test animals. Complete results, Table 26, show a small number of test animals and the low tumor response in the positive control rats.

Manville (1991b) used 2 mg each of four different RCFs for intratracheal instillation to Fischer rats. Lung tumors (adenoma or carcinoma) were found in 6/109 kaolin, 4/107 zirconium, 4/109 high purity RCF and 7/108 after-service RCF (27% crystalline silica content). Positive controls (0.66 mg chrysotile asbestos suspension) had 8/55 tumors, with 0/118 in negative (saline) controls. The authors also noted 1/107 pleural mesotheliomas in the zirconium test animals.

Intrapleural Administration

Stanton *et al.* (1981) administered single doses of ceramic fibers to rats using intrathoracic implantations. There were 13 different RCF of varying dimensions. After two years, pleural sarcoma production ranged from 1/28 to 15/24 (aluminum oxide fiber).

Table 26. RCF intratracheal instillation study results in rats and hamsters

	Hamsters		Rats	
Test Material	Fibrosis	Primary Tumors	Fibrosis	Primary Tumors
RCF	4/25	0/25	2/22	0/22
Crocidolite controls	23/27	20/27	24/25	2/25
Saline (negative) controls	0/24	0/24	1/25	0/25
Cage Controls	3/112	0/112	17/125	0/125

Three pleural mesotheliomas developed when 31 SPF Wistar test rats were injected with 20 mg of aluminum silicate ceramic fibers (0.5-1.0 Fm diameter; length not given). Chrysotile controls had mesotheliomas in 21/32 and 23/36 animals. Negative control rates were 0/48 and 0/32 (Wagner *et al.*, 1973).

Another study was published by Pigott and Ishmael (1982), who injected rats with 20 mg of Saffril® fibers (>95% alumina, 3-4% silica). No mesotheliomas developed over the life of the test animals, whereas chrysotile control animals had 7 mesotheliomas (48 animals).

Intraperitoneal Injection

Low tumor incidence from ceramic fibers was found when Smith *et al.* (1987) injected Syrian hamsters with 25 mg RCF dust (86% <2 Fm diameter; 83% >10 Fm long). Peritoneal mesotheliomas were found in 2/15 and 5/21 test animals. Neither of the negative control groups (saline and cage) developed tumors. There were 8 abdominal mesotheliomas in 25 crocidolite controls.

Similar results were obtained when SPF Wistar rats received single 25 mg injections of fibrous ceramic aluminum silicate glass, where 90% of the fibers were <0.3 Fm in diameter and <3 Fm long. After 850 days, 3/32 test animals developed peritoneal tumors - 1 mesothelioma and 2 fibrosarcomas. No negative controls were used, and the authors note that the challenge fibers were very short (Davis *et al.*, 1984).

Conflicting results were published by the Smith *et al.* (1987) study for intraperitoneal injection in Osborne-Mendel rats. In this case, 19/23 test animals had mesotheliomas - results quite different from the findings of Davis *et al*. Mesotheliomas were found in 20/25 crocidolite controls, 0/25 saline controls and 0/125 cage controls.

Pott *et al.* (1987) injected Wistar rats with two different ceramic wools for five weeks - 9 mg Fiberfrax® (Carborundum ceramic wool; total 45 mg dose) and 15 mg MAN (Manville ceramic wool; total dose 75 mg) - having approximately the same median measurements (Fiberfrax® - 50% <0.89 Fm diameter and <13 Fm long; MAN - 50% <1.4 Fm diameter and <16 Fm long). Reported 130 weeks after injection, Fiberfrax® animals had 33/47 tumors and MAN animals 12/54. Chrysotile controls had peritoneal tumors at 12/36, 23/34 and 30/36 with doses of 0.05 mg, 0.25 mg and 1.0 mg, respectively. Negative (saline) controls had 2/102 tumors.

Pott *et al.* (1989) repeated the experiment, using the same two RCF wools, as well as 12 other fiber types that were not considered MMVF. The results for the ceramic fibers were almost identical to the previous findings. Tumor rates (mesothelioma or sarcoma) in female Wistar rats were 33/47 for Fiberfrax® and 12/54 for MAN. Chrysotile control rates were 12/36, 23/34 and 30/36 (0.05mg, 0.25 mg and 1.0 mg doses), with saline controls (negative) having 1/102 peritoneal tumors. This study also assessed fiber size in relation to carcinogenicity. Based on their experimental results, Pott *et al.* stated that the maximum fiber potency is probably not exhibited until fibers are at least about 20 Fm long.

Another study by Pott *et al.* (1991) tested four RCF samples in female Wistar rats: single 12 mg dose of Fiberfrax I (median diameter 0.47 Fm x length 5.5 Fm); single 12 mg dose of Fiberfrax II (median diameter 0.84 Fm x length 13.1Fm); two weekly doses of 20 mg each Fiberfrax II; and two weekly doses of 20 mg each Manville5 (median diameter 1.35 Fm x length 16.4 Fm). Results for peritoneal mesotheliomas or sarcomas after 131 weeks were: 15/35, 17/36, 29/36 and 6/36, respectively. Negative controls showed 0/34 tumors (50-1 ml injections of saline). Crocidolite controls had 1/34 tumors and chrysotile rats had 0/31 tumors. The authors note that positive controls were injected subcutaneously, and tumors reported are for sarcoma at the injection site. Test animal tumors were for either mesothelioma or sarcoma in the abdominal cavity.

Inhalation

Davis *et al.* (1984) exposed Wistar rats to 10 mg/m^3 respirable fibrous ceramic aluminum silicate glass (90% <0.3 Fm diameter and >3 Fm long; airborne dose of fibers >5 Fm long = 95 f/ml). Exposures occurred at the rate of 7 hours a day, 5 days per week, for 224 days. Eight of 48 test animals developed tumors (1 benign adenoma, 3 carcinomas, 4 histiocytomas). Untreated controls were all negative. Based on histological examination, the study theorized that the tumors were the result of the short, thin fibers, since these were the only particles seen intracellularly. Apparently the other fibers had already been cleared from the alveoli. This theory was supported by RCF clearance rate studies in guinea pigs done by Hammad and Attieh (1989).

Pigott *et al.* (1981) reported no pulmonary fibrosis and no increase in lung cancers (when compared with controls) when rats were exposed to refractory alumina fibers. Pigott and Ishmael (1982) exposed rats to dust clouds of Saffril® (>95% alumina, 3-4% silica) with a median diameter of 3.3 Fm and to aged

refractory alumina. No pulmonary tumors were found with either ceramic fiber. Chrysotile controls (39) developed 9 tumors. However, the overall respirable portion of the dust cloud was only 2.5% on average.

Both rats and hamsters were exposed to "ceramic fiber" dust clouds by Smith *et al.* (1984, 1987). Over two years, animals were treated 6 hours per day, 5 days per week, with a 10.8 mg/m^3 nose-only exposure. The fiber diameter mean was 1.8 Fm, with 83% >10 Fm long. For rats, neither the test (0/55) nor the negative control animals developed lung tumors, while 3/57 crocidolite controls were positive for tumors (1 mesothelioma and 2 bronchoalveolar tumors). In the test hamsters, there was 1 mesothelioma in 70 animals, though there were no lung tumors reported. Hamster controls showed 1 bronchoalveolar tumor in 58 negative (filtered air) controls and 0/58 crocidolite controls. No tumors were reported in either the rat or hamster cage controls. Note the low incidence of tumor induction in the crocidolite asbestos positive controls.

In June 1988, a series of long-term inhalation MMVF studies was initiated by TIMA and contracted to a Switzerland research firm, Research and Consulting Company (RCC), Geneva. One of the goals was to resolve the conflicting results obtained by Davis *et al.* (1984) and Smith *et al.* (1987) for RCF, though the study was later extended to include glass and mineral wools. In the RCF maximum tolerated dose (MTD) study, male Fischer 344 rats were exposed nose-only to one of four ceramic fibers: RCF1 - kaolin (0.82 Fm diameter x 15.9 Fm long); RCF2 - alumina silica zirconoid (0.88 Fm x 12.8 Fm); RCF3 - high purity (0.85 Fm x 17.4 Fm); and RCF4 - after-service kaolin RCF (1.22 Fm x 9.8 Fm; contained 27% crystalline silica after exposure to high temperature). All fiber dimensions are geometric means of the aerosol. Animal exposures were at the MTD of 30 mg/m^3 (approximately 220 f/cc) for 6 hours a day, 5 days per week for 24 months. The MTD value resulted from short-term acute studies done specifically to determine the maximum dose that test animals could be exposed to without severely limiting their ability to breath. Chrysotile asbestos (10 mg/m^3; 0.08 Fm x 1.2 Fm) was used as the positive control; filtered air was the negative control. Interim animal sacrifices were made at three month intervals, with remaining animals observed for their lifetime or until 20% survival of the test group (about 30 months post-exposure). Groups of 3 rats each were also removed from the exposure groups at 3, 6, 9, 12 and 18 months. These recovery group animals were held without further exposure until sacrificed at 24 months.

Final results showed statistically significant increases in lung neoplasms (adenomas or carcinomas) in the first three test exposure groups when compared with air controls: kaolin (RCF1) - 16/123; zirconium (RCF2) - 9/121; high purity (RCF3) - 19/121; after-service (RCF4) - 4/118; negative control - 2/130; and chrysotile control - 13/69. Further, the studies reported 2 pleural mesotheliomas in the kaolin, 3 in zirconium, 2 in high purity and 1 in after-service test groups (1 mesothelioma in chrysotile control, 0 in negative control). These results, though not statistically different from the negative control, were noted because mesotheliomas are not known to occur spontaneously in rats. All mesotheliomas occurred between 24 and 30 months. The study also found that kaolin and high purity RCF test animals developed lung fibrosis in 6 months, zirconium RCF animals in 9 months and after-service RCF animals in 12 months. Chrysotile controls showed lung fibrosis at the 3 month sacrifice. Lung fiber burden evaluations showed that RCF did reach and were retained in the deep lung, with the plateau at about 12 months. There was

almost no change in lung-retained fiber dimensions, suggesting that RCF do not biodegrade even after reaching the deep lung. The authors also noted significant fiber clearing in animals removed from exposures (recovery groups) (Manville, 1991a, 1991b; Hesterberg *et al*., 1991b; Glass *et al*., 1992; Bunn *et al.*, 1993a; Hesterberg *et al*., 1993; Mast *et al*., 1995a; Carborundum Company, 1994a; McConnell *et al*., 1995).

Mast *et al.* (1993) reported a RCF study done concurrently with the Hesterberg *et al*. (1993) glass wool work, where they used the same animal source and test facilities. Mast *et al*. exposed rats to RCF1 (kaolin) only, at 30 mg/m^3 (. 234 f/cc) for 6 hours/day, 5 days/week for 24 months. The RCF aerosol fibers were sized at 0.82 Fm diameter x 15.9 Fm long (geometric mean). There was a statistically significant increase in lung tumors of exposed rats - 16/123 (8 adenomas, 8 carcinomas) with 2 mesotheliomas. Pulmonary fibrosis was noted at 6 months. Chrysotile controls (10 mg/m^3 of fibers sized at 0.08 Fm diameter x .2 Fm long) had tumors of 13/69 (7 adenomas, 6 carcinomas) with 1 mesothelioma. The tumor rate for negative (air) control animals was 4/123 (3 adenomas, 1 carcinoma).

Concurrent MTD studies were done with Syrian hamsters using only RCF1 (kaolin), but with same exposure parameters (30 mg/m^3, 6 hours/day, 5 days/week) for 18 months. Animals were sacrificed at three month intervals. Results showed no lung neoplasms, but 43/102 malignant mesotheliomas in test animals, no tumors in 80 chrysotile controls and 0/73 filtered air (negative) controls. The authors reported pulmonary interstitial fibrosis in RCF animals beginning 9 months after exposure, though there was little additional progression of the fibrosis through the end of the study (Carborundum Company, 1990; Hesterberg *et al*., 1991a; Bunn *et al*., 1993a; Carborundum Company, 1994a; McConnell *et al*., 1995).

The multi-dose inhalation component of the RCC studies were done to determine dose-response relationships and to look for the no observed adverse effect level, or NOAEL, the highest dose that did not produce disease. In these studies, Fischer 344 rats were exposed to 3, 9, and 16 mg/m³ of kaolin RCF for 24 months (approximately 36, 91 and 162 f/cc, respectively). Fibers were about 1 Fm diameter and 20 Fm long. Animals were held until approximately 20% survival, which was at 30 months. In addition to interim sacrifices every 3 months, small groups of 3-6 rats were also removed from exposures at 3, 6, 12 and 18 months and held till terminal sacrifice (recovery controls).

Overall, there was a dose dependent increase seen in pulmonary fibrosis for all test groups. There was no evidence for irreversible lung disease at 3 mg/m³. At 9 mg/m³, there was 1 mesothelioma, with mild parenchymal fibrosis, though there was no noticeable progression after initial appearance. Fibrosis was seen at 12 months for animals exposed at 16 mg/m³. Animals exposed for the full 24 months to the MTD (30 mg/m3) showed continued progression of fibrosis, suggesting that once a critical mass of fibers reaches the pleura, fibers continue to solicit reaction. Authors noted that pulmonary lesions in recovery animals did not progress (become more severe) after animals were removed from exposures.

The multi-dose study results are summarized in Table 27 (Carborundum Company, 1994a; McConnell, 1994; Mast *et al*., 1995b). Results from Mast *et al*. (1993) at 30 mg/m3 are included for comparison.

Table 27. Summary of lesions in rats exposed to RCF1(kaolin) in maximum tolerated dose and multi-dose inhalation studies [Adenoma = non-malignant lung tumor; carcinoma = malignant lung tumor; mesothelioma = malignant pleural tumor]

Exposure Group	No. Animals	Adenomas	Carcinomas	Total Tumors (Percent)	Mesotheliomas
3 mg/m^3	123	2	0	2 (1.6)	0
9 mg/m^3	127	4	1	5 (3.9)	1
16 mg/m^3	124	1	1	2 (1.6)	0
30 mg/m^3	123	8	8	16 (13.0)	2
air control	129	1	0	1 (0.8)	0

CONCLUSIONS

Scientific data shows that MMVF exposures cause fibrosis and an increased risk for non-malignant respiratory disease. Though there is some animal and epidemiological evidence to support fiber carcinogenicity, particularly for the refractory ceramic fibers (RCF), results are not consistent. The scientific community cannot reach consensus on exactly how to interpret the data. The main difficulties include the following:

C Animal study data shows an overall increase in tumor induction when fibers are artificially introduced. The same is not true with inhalation studies.

C There has been little consistency in animal study protocols. Concerns include differences in: exposure doses (percent fiber vs. percent dust; test dose vs. total dose); fiber and/or dust size differences (respirable vs. non-respirable, especially for inhalation studies); exposure method (intrapleural vs. intratracheal vs. intraperitoneal injection and implantation; inhalation nose-only vs. chamber); test animal species (different strains of rat vs. hamster; some data from guinea pigs, monkeys, baboons); length of studies; and small numbers of test animals. Consequently, results from one study are not directly comparable to other studies, though such comparisons have been published.

C Epidemiological data have similar problems. Most studies have been assessments of workers in manufacturing facilities. Problems include confounders that are not adequately addressed (e.g., MMVF workers often had exposures to asbestos or other known stressors and/or were cigarette smokers), inadequate or no air sampling data available, standard mortality ratios based on local vs. national rates, production of more than one type of fiber in the same plant and variations in employment time requirements for the cohort.

Summarizing available data to date, Pigott (1991) listed the following important fiber diameters:

Characteristic	Critical Diameter or Character
Inhalability	<7.5 Fm
Respirability	<3 Fm (<3:1 aspect ratio)
	[.2 Fm at 20:1 aspect ratio]
Skin irritation	<5 Fm is non-irritant
	5 Fm-10 Fm is irritant
	>10 Fm is severe irritant
Fibrogenic potential	non-respirable and short
Mesothelioma induction	<1 Fm (at 5:1 aspect ratio?)
Lung cancer	???

He states that the ideal MMVF production would make a material with fibers greater than 1 Fm in diameter to decrease the chance of mesothelioma, greater than 3 Fm to circumvent respirability issues, but less than 5 Fm so mechanical irritation effects will be limited.

Research efforts continue, focusing on establishing and using reliable animal protocols and on performing additional epidemiological investigations. Meanwhile, following are some general conclusions:

1. Fibrous glass (continuous filament glass [textile glass], continuous filament superfine glass [microfibers; special purpose glass] and glass wool)

The acute health effects of fibrous glass - skin, eye and respiratory irritation - are well documented. Chronic hazards are less clearly defined. Animals artificially exposed to glass wool and glass microfibers by implantation and injection have developed fibrosis, lung cancers and mesothelioma. Inhalation studies have thus far shown no evidence for the fibrogenicity or carcinogenicity of continuous filament glass fibers. Overall, fibrous glass is much less carcinogenic than the crocidolite and chrysotile asbestos controls used in animal studies.

In vitro studies have shown that glass microfibers cause chromosomal aberrations and are cytotoxic.

Epidemiological data is mainly based on manufacturing plants. For continuous glass, there is no evidence of excess lung cancer or of non-malignant respiratory disease. Glass wool data shows an increased risk of lung cancer, though the risk does not appear to be tied directly to either length of exposure or cumulative exposure dose. There is also evidence of excess risk of non-malignant respiratory disease (e.g., rhinitis, pharyngitis, bronchitis and lung opacities) for both production workers and end users.

Results reported for personnel exposures in manufacturing and fabrication of glass textile fibers and wool have been less than 1.5 fibers per cubic centimeter of air (f/cc). Fine glass manufacturing reports higher exposures, up to 4.38 f/cc. There is a single report of a 21.9 f/cc exposure while adding raw fine glass fibers in an unventilated paper mixing operation. End user exposures as high as 3.62 f/cc have been reported for insulators blowing loose fiber fill with no binder.

2. Mineral wool (slag and rock)

Limited rock wool injection studies have shown slight fibrosis (intratracheal only) and mesothelioma. Inhalation data show evidence of fibrogenicity at extremely high fiber concentrations, with no positive findings for carcinogenicity. Animal studies using slag wool report no significant fibrotic or carcinogenic effects.

There is inadequate epidemiological information to correlate mineral wool exposures with non-malignant respiratory disease. Increased risk of respiratory cancer has been demonstrated in workers, but the latest

cohort update states that the risk appears to be less as follow-up continues, particularly for rock wool workers.

The highest reported employee exposure in manufacturing is 1.59 f/cc. Blowing loose mineral wool insulation (no binder) yields the highest end user exposures at 7.8 f/cc.

3. Refractory ceramic fibers (RCF)

Test animals have developed significant pulmonary fibrosis, lung tumors and mesothelioma when exposed by injection, implantation and inhalation.

Limited epidemiological data have shown production workers to be at increased risk for non-malignant respiratory disease, including decreased pulmonary function (statistically significant, especially when associated with exposure duration), high incidence of pleural plaques and increased pleuritic chest pain. There is no epidemiological information on lung cancer or mesothelioma.

Personal exposure sample results are reported up to 8.38 f/cc during manufacture and fabrication operations. Refractory ceramic installation and removal operations resulted in maximum reported exposures of 2.6 f/cc and 24.72 f/cc, respectively. There is one report of a 50 f/cc exposure during after service removal using pneumatic drills and hammers.

An additional concern with RCF comes from its partial conversion to cristobalite (crystalline silica) at temperatures above 1100 EC. Silica is known to cause silicosis in humans and is classified as a human carcinogen by IARC.

To summarize, based on our review of MMVF toxicological and epidemiological information, there is sufficient animal evidence to consider that glass wool, glass microfibers, mineral wools (rock and slag) and refractory ceramic fibers may be carcinogenic. Despite the shortcomings of implantation and injection animal studies, these protocols have historically served as carcinogenicity indicators.

The controversy about MMVF started mainly because they are used for the same purpose as, and are morphologically similar to, asbestos, a known carcinogen. If our concern is that MMVF may cause similar health impairment, it should also follow that our concern focus on the similarities between the fibers and personnel exposures to these fibers. Though current exposure limits are gravimetric (total and respirable "inert" dusts), it seems logical to regulate MMVF as fibers, and the trend in that direction is obvious with the newly adopted TLVs®. The fallacy in using weight to assess respirable fiber exposures is that low gravimetric weight samples can easily contain a high respirable fiber content. Conversely, high weight samples may well have very few respirable fibers.

REFERENCES

ACGIH (American Conference of Governmental Industrial Hygienists). 1996 TLVs® and BEIs®. Threshold Limit Values for Chemical Substances and Physical Agents. Biological Exposure Indices. ISBN 1-882417-13-5. Cincinnati, OH: ACGIH. 1996.

ACGIH. 1997 TLVs® and BEIs®. Threshold Limit Values for Chemical Substances and Physical Agents. Biological Exposure Indices. ISBN 1-882417-19-4. Cincinnati, OH: ACGIH. 1997.

Adachi, S., Takemoto, K., and Kimura, K. Tumorigenicity of Fine Man-Made Fibers After Intratracheal Administration to Hamsters. Environ. Res. 54(1):52-73 (1991).

Adachi, S., Kawamura, K., Kimura, K., and Takemoto, K. Tumor Incidence Was Not Related to the Thickness of Visceral Pleura in Female Syrian Hamsters Intratracheally Administered Amphibole Asbestos or Manmade Fibers. Environ. Res. 58(1):55-65 (1992).

Antonsson, A. and Runmark, S. Airborne Fibrous Glass and Dust Originating From Worked Reinforced Plastics. Am. Ind. Hyg. Assoc. J. 48(8):684-687 (1987).

Balzer, J. L. Environmental Data; Airborne Concentrations Found in Various Operations. Occupational Exposure to Fibrous Glass. Proceedings of a Symposium. June 26-27, 1974. College Park, MD. HEW Pub. No. (NIOSH) 76-151. 1976. pp. 82-89.

Baron, P. A. and Shulman, S. A. Evaluation of the Magiscan Image Analyzer for Asbestos Fiber Counting. Am. Ind. Hyg. Assoc. J. 48(1):39-46 (1987).

Bauer, J. F., Law, B. D., and Hesterberg, T. W. Dual pH Durability Studies of Man-Made Vitreous Fiber (MMVF). Environ. Health Perspect. 102(Suppl. 5):61-65 (1994).

Bayliss, D. L., Dement, J. M., Wagoner, J. K., and Blejer, H. P. Mortality Patterns Among Fibrous Glass Production Workers. Ann. N Y Acad. Sci. 271:324-335 (1976).

Bellman, B., Konig, H., Muhle, H., and Pott, F. Chemical Durability of Asbestos and of Man-Made Mineral Fibres *in vivo*. J. Aerosol Sci. 17(3):341-345 (1986).

Bellman, B., Muhle, H., Pott, F., Konig, H., Kloppel, H., and Spurney, K. Persistence of Manmade Mineral Fibres (MMMF) and Asbestos in Rat Lungs. Ann. Occup. Hyg. 31(no. 4B):693-709 (1987).

Bellman, B., Muhle, H., and Pott, F. Study on the Durability of Chemically Different Glass Fibres in Lungs on Rats. Zbl. Hyg. 190:310-314 (1990). [Cited in Pott et al., 1991]

Bender, J. R., Konzen, J. L., and Devitt, G. E. Occupational Exposure, Toxic Properties, and Work Practice Guidelines for Fiber Glass. Akron, OH: American Industrial Hygiene Association. 1991.

Bermudez, E. Recovery of Particles From the Pleural Cavity Using Agarose Casts: A Novel Method for the Determination of Fiber Dose to the Rat Pleura. Inhal. Toxicol. 6(2):115-124 (1994).

Bernstein, D. M., Morscheidt, C., Tiesler, H., Grimm, H.-G., Thévenaz, P., and Teichert, U. Evaluation of the Biopersistence of Commercial and Experimental Fibers Following Inhalation. Inhal. Toxicol. 7(7):1031-1058 (1995).

Bertazzi, P. A., Zocchetti, C., Pesatori, A., Radice, L., and Riboldi, L. Cancer Mortality in a Cohort of Glass Fibre Production Workers. Med. Lav. 75:339-358 (1984). [Cited in IARC, 1988]

BNA. Occupational Safety and Health Reporter. 21(8):230-231 (1991).

Boffetta, P., Saracci, R., Anderson, A., Bertazzi, P. A., Chang-Claude, J., Ferro, G., Fletcher, A. C., Frentzel-Beyme, R., Gardner, M. J., Olsen, J. H., Simonato, L., Teppo, L., Westerholm, P., Winter, P., and Zocchetti, C. Lung Cancer Mortality Among Workers in the European Production of Man-Made Mineral Fibers - a Poisson Regression Analysis. Scand. J. Work Environ. Health. 18(5):279-286 (1992).

Brown, G. M., Cowie, H., Davis, J. M. G., and Donaldson, K. *In vitro* Assays for Detecting Carcinogenic Mineral Fibers: A Comparison of Two Assays and the Role of Fiber Size. Carcinogenesis. 7:1971-1974 (1986).

Brown, R. C., Chamberlain, M., Davies, R., Gaffen, J., and Skidmore, J. W. *In vitro* Biological Effects of Glass Fibres. J. Environ. Pathol. Toxicol. 2:1369-1383 (1979a).

Brown, R. C., Chamberlain, M., and Skidmore, J. W. *In vitro* Effects of Man-Made Mineral Fibres. Ann. Occup. Hyg. 22:175-179 (1979b).

Brown, R. C., Davis, J. M. G., Douglas, D., Gruber, U. F., Hoskins, J. A., Ilgren, E. B., Johnson, N. F., Rossiter, C. E., and Wagner, J. C. Carcinogenicity of the Insulation Wools: Reassessment of the IARC Evaluation. Regul. Toxicol. Pharmacol. 14(1):12-23 (1991).

Brown, S. K. Characterization of the Fiber Diameter Distribution of Synthetic Mineral Fiber Products and Their Dusts. Am. Ind. Hyg. Assoc. J. 53(1):27-33 (1992).

Bunn, W. B., Bender, J. R., Hesterberg, T. W., Chase, G. R., and Konzen, J. L. Recent Studies of Man-Made Vitreous Fibers. Chronic Animal Inhalation Studies. J. Occup. Med. 35(2):101-113 (1993a).

Bunn, W. B., Bender, J. R., Hesterberg, T. W., Chase, G. R., and Konzen, J. L. Synthetic Mineral Fibers - The Authors Reply. J. Occup. Med. 35(12):1175-1177 (1993b).

Burge, P. S., Calvert, I. A., Trethowan, W. N., and Harrington, J. M. Are Respiratory Health Effects Found in Manufacturers of Ceramic Fibres Due to the Dust Rather Than the Exposure to Fibres? Occup. Environ. Med. 52(2):105-109 (1995).

Carborundum Company. Two Year Inhalation Bioassay of Refractory Ceramic Fiber (RCF) in the Rat and Hamster. 8EHQ-0890-0553 Suppl. August 21, 1990. Office of Toxic Substances, U.S. EPA, Washington, DC. 1990.

Carborundum Company. Health and Safe Handling Information on Refractory Ceramic Fibers: Health and Safety Studies of Refractory Ceramic Fibers (RCF). Form C-1320-A, effective 6/91. 1991. 4p.

Carborundum Company. Update of Human Health Studies and Animal Studies on RCF. Letter to Customers from W. P. Kelly, Vice President and General Manager, Carborundum Company, Fibers Division, Niagara Falls, NY. July 16, 1992.

Carborundum Company. Safe Management of Industrial Fiber. Health Studies of Refractory Ceramic Fibers (RCF). Form C-1320-A 5M, effective 2/94. 1994a. 4 p.

Carborundum Company. Letter to Customers from W. P. Kelly, Vice President, Carborundum Company, Fibers Division, Niagara Falls, NY. February 2, 1994b.

Carborundum Company Fibers Division. Workplace Quality News #2. Niagara Falls, NY. August 12, 1991.

Carborundum Company Fibers Division. Workplace Quality News #4. Niagara Falls, NY. October 27, 1992a.

Carborundum Company Fibers Division. Workplace Quality News #5. Niagara Falls, NY. December 21, 1992b.

Carborundum Company Fibers Division. Workplace Quality News #6. Niagara Falls, NY. March 16, 1993.

Carborundum Company Fibers Division. Workplace Quality News #9. Niagara Falls, NY. February 1995.

CAS (Chemical Abstract Service). On-line Database, Available through Chemical Abstract Registry File. Produced by CAS, a division of the American Chemical Society. Accessed October 1997.

Casey, G. Sister-Chromatid Exchange and Cell Kinetics in CHO-K1 Cells, Human Fibroblasts and Lymphoblastoid Cells Exposed *in vitro* to Asbestos and Glass Fibre. Mutat. Res. 116:369-377 (1983).

Chamberlain, M. and Tarmy, E. M. Asbestos and Glass Fibers in Bacterial Mutation Tests. Mutat. Res. 43:159-160 (1977). [Cited in Wheeler, 1990]

Chamberlain, M., Brown, R. C., Davies, R., and Griffiths, D. M. *In vitro* Prediction of the Pathogenicity of Mineral Dusts. Br. J. Exp. Pathol. 60:320-327 (1979).

Cheng, R. T., McDermott, H. J., Gia, G. M., Cover, T. L., and Duda, M. M. Exposures to Refractory Ceramic Fiber in Refineries and Chemical Plants. Appl. Occup. Environ. Hyg. 7(6):361-367 (1992).

Cherrie, J. and Dodgson, J. Past Exposure to Airborne Fibers and Other Potential Risk Factors in the European Man-Made Mineral Fiber Production Industry. Scan. J. Work Environ. Health. 12(Suppl. 1):26-33 (1986).

Cherrie, J., Dodgson, J., Groat, S., and Maclaren, W. Environmental Surveys in the European Man-Made Mineral Fiber Production Industry. Scan. J. Work Environ. Health. 12(Suppl. 1):18-25 (1986).

Chiazze, L. Jr. and Watkins, D. K. Epidemiological Studies of Synthetic Vitreous Fibers: Methods Used and Current Studies. Regul. Toxicol. Pharmacol. 20:S58-S67 (1994).

Chiazze, L. Jr., Watkins, D. K., and Fryar, C. A Case-Control Study of Malignant and Non-Malignant Respiratory Disease Among Employees of a Fiberglass Manufacturing Facility. B. J. Ind. Med. 49:326-331 (1992).

Chiazze, L. Jr., Watkins, D. K., Fryar, C., and Kozono, J. A Case-Control Study of Malignant and Non-Malignant Respiratory Disease Among Employees of a Fiberglass Manufacturing Facility. II. Exposure Assessment. Br. J. Ind. Med. 50(8):717-725 (1993).

Chiazze, L. Jr., Watkins, D. K., and Fryar, C. Adjustment for the Confounding Effect of Cigarette Smoking in a Historical Cohort Mortality Study of Workers in a Fiberglass Manufacturing Facility. J. Occup. Environ. Med. 37(6):744-748 (1995).

Christensen, D. Exposure Assessment Results - Manufacturing Facilities. Report Given at Johns Hopkins University School of Hygiene and Public Health Symposium. Man-Made Mineral Fibers: Status of Health Risk Assessment, Baltimore, MD. March 4-5, 1991.

Christensen, V. R., Eastes, W., Hamilton, R. D., and Struss, A. W. Fiber Diameter Distributions in Typical MMVF Wool Insulation Products. Am. Ind. Hyg. Assoc. J. 54(5):232-238 (1993).

Claude, J. and Frentzel-Beyme, R. Mortality of Workers in a German Rock Wool Factory - A Second Look with Extended Follow-up. Scan. J. Work Environ. Health. 12(Suppl. 1):53-60 (1986).

CNO (Chief of Naval Operations). Navy Occupational Safety and Health (NAVOSH) Program Manual. OPNAVINST 5100.23D. Washington, DC: CNO. 1994.

Collier, C. G., Morris, K. J., Launder, K. A., Humphreys, J. A., Morgan, A., Eastes, W., and Townsend, S. The Behavior of Glass Fibers in the Rat Following Intraperitoneal Injection. Regul. Toxicol. Pharmacol. 20:S89-S103 (1994).

Corn, M. and Sansone, E. B. Determination of Total Suspended Particulate Matter and Airborne Fiber Concentration at 3 Fibrous Glass Manufacturing Facilities. Environ. Res. 8(no. 1):37-52 (1974).

Corn, M., Hammad, Y. Y., Whittier, D., and Kotsko, N. Employee Exposure to Airborne Fiber and Total Particulate Matter in Two Mineral Wool Facilities. Environ. Res. 12:59-74 (1976).

Davies, L. and Cherrie, J. W. Airborne Fibre Concentrations in a Glass Continuous Filament Factory. Ann. Occup. Hyg. 36(6):609-627 (1992).

Davies, R. The Effect of Mineral Fibres on Macrophages. Biological Effects of Mineral Fibres. Proceedings of a Symposium, vol. 1, edited by J. C. Wagner. September 25-27, 1979. Lyon, France. IARC Scientific Pub. No. 30. 1980. pp. 419-425.

Davis, J. M. G. A Review of Experimental Evidence for the Carcinogenicity of Man-Made Vitreous Fibers. Scan. J. Work Environ. Health. 12(Suppl. 1):12-17 (1986).

Davis, J. M. G., Addison, J., Bolton, R. E., Donaldson, K., Jones, A. D., and Wright, A. The Pathogenic Effects of Fibrous Ceramic Aluminum Silicate Glass Administered to Rats by Inhalation or Peritoneal Injection. Biological Effects of Man-Made Mineral Fibres. Proceedings of a WHO/IARC Conference, vol. 2. April 20-22, 1982. Copenhagen, Denmark. 1984. pp. 303-322.

Dement, J. M. Environmental Aspects of Fibrous Glass Production and Utilization. Environ. Res. 9:295-312 (1975).

Doll, R. Symposium on MMMF, Copenhagen, October 1986: Overview and Conclusions. Ann. Occup. Hyg. 31(no. 4B):805-819 (1987).

Drew, R. T., Kuscher, M., and Bernstein, D. M. The Chronic Effects of Exposure of Rats to Sized Glass Fibres. Ann. Occup. Hyg. 31(no. 4B):711-729 (1987).

Eastes, W., Morris, K. J., Morgan, A., Launder, K. A., Collier, C. G., Davis, J. A., Mattson, S. M., and Hadley, J. G. Dissolution of Glass Fibers in the Rat Lung Following Intratracheal Instillation. Inhal. Toxicol. 7:197-312 (1995).

Engholm, G., Englund, A., Fletcher, A. C., and Hallin, N. Respiratory Cancer Incidence in Swedish Construction Workers Exposed to Man-Made Mineral Fibers and Asbestos. Ann. Occup. Hyg. 31 (no. 4B):663-675 (1987).

Enterline, P. E. Role of Manmade Mineral Fibres in the Causation of Cancer (editorial). Br. J. Ind. Med. 47(3):145-146 (1990a).

Enterline, P. E. Role of Manmade Mineral Fibres in the Causation of Cancer (Author's Reply). Br. J. Ind. Med. 47(9):646-647 (1990b).

Enterline, P. E. and Marsh, G. M. The Health of Workers in the MMMF Industry. Biological Effects of Man-Made Mineral Fibres. Proceedings of a WHO/IARC Conference, vol. 1. April 20-22, 1982. Copenhagen, Denmark. 1984. pp. 311-339.

Enterline, P. E., Marsh, G. M., and Esmen, N. A. Mortality Among Man-Made Mineral Fiber Workers in the United States. Prepared for the Medical and Science Committee of the TIMA. 1981.

Enterline, P. E., Marsh, G. M., and Esmen, N. A. Respiratory Disease Among Workers Exposed to Man-Made Mineral Fibers. Am. Rev. Respir. Dis. 128:1-7 (1983).

Enterline, P.E., Marsh, G. M., Henderson, V., and Callahan, C. Mortality Update of a Cohort of US Man-Made Mineral Fibre Workers. Ann. Occup. Hyg. 31(no. 4B):625-656 (1987).

EPA (Environmental Protection Agency). Final Action. Testing Consent Order for Refractory Ceramic Fibers. Federal Register 58:92 of 14 May 1993. p. 28517-28520.

EPA. Refractory Ceramic Fiber; Proposed Significant New Use of a Chemical Substance. Federal Register 59:54 of 21 Mar 1994a. p. 13294-13298.

EPA. Refractory Ceramic Fiber; Proposed Significant New Use of a Chemical Substance. Federal Register 59:235 of 8 Dec 1994b. p. 63299-63300.

EPA. Code of Federal Regulations, Title 40. 1996 or latest revision. [Part 60, Sections 290-296, Subpart CC; Part 60, Sections 680-685, Subpart PPP; Part 261; Part 426, Subpart A; Part 721, Subpart E; Part 799, Section 5000.]

Esmen, N. A. Short-term Survey of Airborne Fibres in US Manufacturing Plants. Biological Effects of Man-Made Mineral Fibres. Proceedings of a WHO/IARC Conference, vol. 1. April 20-22, 1982. Copenhagen, Denmark. 1984. pp. 65-82.

Esmen, N. A., Hammad, Y. Y., Corn, M., Whittier, D., Kotsko, N., Haller, M., and Kahn, R. A. Exposure of Employees to Man-Made Mineral Wool Production. Environ. Res. 15:262-277 (1978).

Esmen, N., Corn, M., Hammad, Y. Y., Whittier, D., and Kotsko, N. Summary of Measurements of Employee Exposure to Airborne Dust and Fiber in Sixteen Facilities Producing Man-Made Mineral Fibers. Am. Ind. Hyg. Assoc. J. 40:108-117 (1979a).

Esmen, N. A., Corn, M., Hammad, Y. Y., Whittier, D., Kotsko, N., Haller, M., and Kahn, R. A. Exposure of Employees to Man-Made Mineral Fibers: Ceramic Fiber Production. Environ. Res. 19:265-278 (1979b).

Esmen, N., Sheehan, M,. Corn, M., Engel, M., and Kotsko, N. Exposure of Employees to Man-Made Vitreous Fibers: Installation of Insulation Material. Environ. Res. 28:386-398 (1982).

Everitt, J. I. Mechanisms of Fiber-Induced Diseases: Implications for the Safety Evaluation of Synthetic Vitreous Fibers. Regul. Toxicol. Pharmacol. 20:S68-S75 (1994).

Fallentine. Historical Survey of the Industrial Hygiene Conditions in Rock Wool/Slag Wool Producing Plants - Simulation of Rock Wool/Slag Wool Production in the Early Technological Phase. Joint European Medical Research Board. 1990. [Cited in TIMA, 1990]

Förster, H. The Behavior of Mineral Fibres in Physiological Solution. Biological Effects of Man-Made Mineral Fibres. Proceedings of a WHO/IARC Conference, vol. 2. April 20-22, 1982. Copenhagen, Denmark. 1984. pp. 27-59.

Fowler, D. P., Balzer, L. J., and Cooper, W. C. Exposure of Insulation Workers to Airborne Fibrous Glass. Am. Ind. Hyg. Assoc. J. 32:86-91 (1971).

Friar, J. J. and Phillips, A.M. Exposure to Ceramic Man-Made Mineral Fibres. In: Non-Occupational Exposure to Mineral Fibres, edited by J. Bignon, J. Peto, and R. Saracci. IARC Scientific Pub. No. 90. Lyon: IARC. 1989. pp. 299-303.

Gantner, B.A. Respiratory Hazard From Removal of Ceramic Fiber Insulation From High Temperature Industrial Furnaces. Am. Ind. Hyg. Assoc. J. 47(8):530-534 (1986).

Gaudichet, A., Petit, G., Billon-Galland, M. A., and Dufour, G. Levels of Atmospheric Pollution by Man-Made Mineral Fibres in Buildings. In: Non-Occupational Exposure to Mineral Fibres, edited by J. Bignon, J. Peto, and R. Saracci. IARC Scientific Pub. No. 90. Lyon: IARC. 1989. pp. 291-298.

Glass, L. R., Mast, R. W., Hesterberg, T. H., Anderson, R., McConnell, E. E., and Bernstein, D. M. Inhalation Oncogenicity Study of Refractory Ceramic Fiber (RCF) in Rats - Final Results. Toxicologist. 12:377 (1992).

Goldsmith, J. R. and Goldsmith, D. F. Fiberglass or Silica Exposure and Increased Nephritis or ERSD (End-Stage Renal Disease). Am. J. Ind. Med. 23(6):873-881 (1993).

Goldstein, B., Rendall, R. E. G., and Webster, I. A Comparison of the Effects of Exposure of Baboons to Crocidolite and Fibrous Glass Dusts. Environ. Res. 32:344-359 (1983).

Goldstein, B., Webster, I., and Rendall, R. E. G. Changes Produced by the Inhalation of Glass Fibre in Non Human Primates. Biological Effects of Man-Made Mineral Fibres. Proceedings of a WHO/IARC Conference, vol. 2. April 20-22, 1982. Copenhagen, Denmark. 1984. pp. 273-285.

Gormley, I. P., Brown, G. M., Cowie, H., Wright, A., and Davis, J. M. G. The Effects of Fiber Length on the *in vitro* Cytology of Asbestos Samples in Three Different Assay Systems. In: *In vitro* Effects of Mineral Dusts, edited by E. G. Beck and J. Bignon. New York: Springer-Verlag. 1985. pp. 397-404.

Gross, P., Kaschak, M., Tolker, E. B., Fabyak, M. A., and deTreville, R. T. P. The Pulmonary Reaction to High Concentrations of Fibrous Glass Dust. Arch. Environ. Health. 20:696-704 (1970).

Gustavsson, P., Plato, N., Axelson, O., Brage, H. N., Hogstedt, C., Ringbäck, G., Tornling, G., and Wingren, G. Lung Cancer Risk Among Workers Exposed to Man-Made Mineral Fibers (MMMF) in the Swedish Prefabricated House Industry. Am. J. Ind. Med. 21:825-834 (1992).

Hammad, Y. Y. Deposition and Elimination of MMMF. Biological Effects of Man-Made Mineral Fibres. Proceedings of a WHO/IARC Conference, vol. 2. April 20-22, 1982. Copenhagen, Denmark. 1984. pp. 126-142.

Hammad, Y. Y. Effect of Chemical Composition on Pulmonary Clearance of Man-Made Mineral Fibers. Ann. Occup. Hyg. 32:769-770 (1988).

Hammad, Y. Y. and Attieh, B. Pulmonary Deposition of MMMF. J. Aerosol Sci. 20(8):1329-1332 (1989).

Hammad, Y. Y. and Esmen, N. A. Long-Term Survey of Airborne Fibres in the United States. Proceedings of a WHO/IARC Conference, vol. 1. April 20-22, 1982. Copenhagen, Denmark. 1984. pp. 118-132.

Hammad, Y., Diem, J., Craighead, J., and Weill, H. Deposition of Inhaled Man-Made Mineral Fibres in the Lungs of Rats. Ann. Occup. Hyg. 26(1,4):179-187 (1982).

Harris, R. L. and Timbrell, V. The Influence of Fibre Shape in Lung Deposition - Mathematical Estimates. In: Inhaled Particles IV, edited by W. H. Walton. Oxford: Pergamon Press. 1977. pp. 75-89.

Hart, G. A., Kathman, L. M., and Hesterberg, T. W. *In vitro* Cytotoxicity of Asbestos and Man-Made Vitreous Fibers: Roles of Fiber Length, Diameter and Composition. Carcinogenesis. 15(5):971-977 (1994).

Head, I. W. H and Wagg, R. M. A Survey of Occupational Exposure to Man-Made Mineral Fiber Dust. Ann. Occup. Hyg. 23(3):235-258 (1980).

Hesterberg, T. W. and Barrett, J. C. Dependence of Asbestos and Mineral Dust in Transformation of Mammalian Cells in Culture on Fibre Dimension. Cancer Res. 44:2170-2180 (1984).

Hesterberg, T. W. and Hart, G. A. A Comparison of Human Exposures to Fiberglass with Those Used in a Recent Rat Chronic Inhalation Study. Regul. Toxicol. Pharmacol. 20:S35-S46 (1994).

Hesterberg, T. W., Mast, R., McConnell, E. E., Chevalier, J., Bernstein, D. M., Bunn, W. B., and Anderson, R. Chronic Inhalation Toxicity of Refractory Ceramic Fibers in Syrian Hamsters. In: Mechanisms in Fibre Carcinogenesis, edited by R. C. Brown, J. A. Hoskins, and N. F. Johnson. New York: Plenum Press. 1991a. pp. 531-538.

Hesterberg, T. W., Mast, R., McConnell, E. E., Vogel, O., Chevalier, J., Bernstein, D. M., and Anderson, R. Chronic Inhalation Toxicity and Oncogenicity Study of Refractory Ceramic Fibers in Fischer 344 Rats. Toxicologist. 11:254 (1991b).

Hesterberg, T. W., Miiller, W. C., McConnell, E. E., Chevalier, J., Hadley, J. G., Bernstein, D. M., Thevenaz, P., and Anderson, R. Chronic Inhalation Toxicity of Size-Separated Glass Fibers in Fischer 344 Rats. Fundam. Appl. Toxicol. 20(4):464-476 (1993).

Hill, J. W. Man-Made Mineral Fibres and Lung Disease. Chem. Ind. 182-184 (1980).

Hill, J. W., Whitehead, W. S., Cameron, J. D., and Hedgecock, G. A. Glass Fibres: Absence of Pulmonary Hazard in Production Workers. Br. J. Ind. Med. 30:174-179 (1973).

Hook, H. L., Morrice, Jr., G., and deTreville, R. T. Fiberglass Manufacturing and Health: Results of a Comprehensive Physiological Study. Proceedings of the 35th Annual Meeting of the Industrial Health Foundation. October 13-14, 1970. Pittsburgh, PA. IHF Bulletin No. 44. 1970. 103-111.

Hughes, J. M., Jones, R. N., Glindmeyer, H. W., Hammad, Y. Y., and Weill, H. Follow Up Study of Workers Exposed to Man Made Mineral Fibres. Br. J. Ind. Med. 50(7):658-667 (1993).

IARC (International Agency for Research on Cancer). IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans: Silica and Other Silicates, vol. 42. UK: IARC. 1987.

IARC. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Man-Made Mineral Fibres and Radon, vol. 43. UK: IARC. 1988.

IARC. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Silica, Some Silicates, Coal Dust and para-Aramid Fibrils, vol. 68. UK: IARC. 1996.

Indulski, J., GoÑcicki, J., Wiecek, E., and Stroszejn-Mrowca, G. The Evaluation of Occupational Exposure of Workers to Airborne MMMF in Poland. Biological Effects of Man-Made Mineral Fibres. Proceedings of a WHO/IARC Conference, vol. 1. April 20-22, 1982. Copenhagen, Denmark. 1984. pp. 191-197.

Infante, P. F., Schuman, L. D., Dement, J., and Huff, J. Commentary. Fibrous Glass and Cancer. Am. J. Ind. Med. 26:559-584 (1994).

ILO (International Labor Organization). Safety in the Use of Mineral Synthetic Fibres. Occupational Safety and Health Series 64. 3rd ed. Geneva: ILO. 1990. pp. 62-64.

IRIS (Integrated Risk Information System). Refractory Ceramic Fibers Carcinogenicity Assessment, 07/01/93. On-Line Database Available through National Library of Medicine. Produced by the U.S. Environmental Protection Agency. Accessed 10 June 1997.

Jacob, T. R., Hadley, J. G., Bender, J. R., and Eastes, W. Airborne Glass Fiber Concentrations During Manufacturing Operations Involving Glass Wool Insulation. Am. Ind. Hyg. Assoc. J. 54(6):320-326 (1993).

Jaffrey, J. S. A. M. Levels of Airborne Man-Made Mineral Fibres in U. K. Dwellings. I - Fibre Levels During and After Installation of Insulation. Atmos. Environ. 24A(1):133-141 (1990).

Jaffrey, J. S. A. M., Rood, A. P., Llewellyn, J. W., Wilson, A. J. Levels of Airborne Man-Made Mineral Fibres in U. K. Dwellings. II - Fibre Levels During and After Some Disturbance of Loft Insulation. Atmos. Environ. 24A(1):143-146 (1990).

Johnson, N. F. An Overview of Animal Models for Assessing Synthetic Vitreous Fibers (SVF) Safety. Regul. Toxicol. Pharmacol. 20:S7-S21 (1994).

Johnson, N. F., Griffiths, D. M., and Hill, R. J. Size Distribution Following Long Term Inhalation of MMMF. Biological Effects of Man-Made Mineral Fibres. Proceedings of a WHO/IARC Conference, vol. 2. April 20-22, 1982. Copenhagen, Denmark. 1984. pp. 102-105.

Kojola, W. H. and Moran, J. B. Commentary. Exposure Limits for Man-Made Mineral Fibers. Position of the Building and Construction Trades Department, AFL-CIO. Appl. Occup. Environ. Hyg. 7(11):724-733 (1992).

Konzen, J. L. Results of Environmental Air Sampling Studies Conducted in Owens-Corning Fiberglas Manufacturing Plants. Occupational Exposure to Fibrous Glass. A Symposium. June 26-27, 1974. College Park, MD. HEW Pub. No. (NIOSH) 76-151. 1976. pp. 115-120.

Koshi, K., Kohyama, N., Myojo, T., and Fukuda, K. Cell Toxicity, Hemolytic Action and Clastogenic Activity of Asbestos and Its Substitutes. Ind. Health. 29(2):37-56 (1991).

Kotin, P. Pathophysiology in Relation to the Chemical and Physical Properties of Fibers. Proceedings of the Workshop on Asbestos: Definitions and Measurement Methods. July 18-20, 1977. Gaithersburg, MD. 1978. pp. 133-142.

Krantz, S. Exposure to Man-Made Mineral Fibers at Ten Production Plants in Sweden. Scand. J. Work Environ. Health. 14(Suppl. 1):49-51 (1988).

Law, B. D., Bunn, W. B., and Hesterberg, T. W. Solubility of Polymeric Organic Fibers and Man Made Vitreous Fibers in Gambles Solution. Inh. Toxicol. 2:321-339 (1990).

Leanderson, P. and Tagesson, C. Cigarette Smoke Potentiates the DNA-Damaging Effect of Manmade Mineral Fibers. Am. J. Ind. Med. 16:697-706 (1989).

Leanderson, P. and Tagesson, C. Hydrogen Peroxide Release and Hydroxyl Radical Formation in Mixtures Containing Mineral Fibres and Human Neutrophils. Br. J. Ind. Med. 49(11):745-749 (1992).

LeBouffant, L., Henin, J. P., Martin, J. C., Normand, C., Tichoux, G., and Trolard, F. Distribution of Inhaled MMMF in Rat Lung - Long Term Effects. Biological Effects of Man-Made Mineral Fibres. Proceedings of a WHO/IARC Conference, vol. 2. April 20-22, 1982. Copenhagen, Denmark. 1984. pp. 143-168.

LeBouffant, L., Daniel, H., Henin, J. P., Martin, J. C., Normand, C., Tichour, G., and Trolard, F. Experimental Study on Long-Term Effects of Inhaled MMMF on the Lungs of Rats. Ann. Occup.

Hyg. 31 (no. 4B):765-790 (1987).

Lee, K. P., Barras, C. E., Griffith, F. D., Waritz, R. S., and Lapin, C. A. Comparative Pulmonary Responses to Inhaled Inorganic Fibers with Asbestos and Fiberglass. Environ. Res. 24:167-191 (1981).

Lee, I.-M., Hennekens, C. H., Trichopoulos, D., and Buring, J. E. Man-Made Vitreous Fibers and Risk of Respiratory System Cancer: A Review of the Epidemiological Evidence. J. Occup. Environ. Med. 37(6):725-738 (1995).

Lees, P. S. J. Exposure Assessment Results - End Users. Presentation at Man-Made Mineral Fibers: Status of Health Risk Assessment. March 4-5, 1991. Baltimore, MD. 1991.

Lees, P. S. J., Breysse, P. N., McArthur, B. R., Miller, M. E., Rooney, B. C., Robbins, C. A., and Corn, M. End User Exposures to Man-Made Vitreous Fibers: I. Installation of Residential Insulation Products. Appl. Occup. Environ. Hyg. 8(12):1022-1030 (1993).

Leineweber, J. P. Solubility of Fibres *in vitro* and *in vivo*. Biological Effects of Man-Made Mineral Fibres. Proceedings of a WHO/IARC Conference, vol. 2. April 20-22, 1982. Copenhagen, Denmark. 1984. pp. 87-101.

Lemasters, G. and Lockey, J. Radiographic Changes Among Workers Manufacturing Refractory Ceramic Fibre and Products. Ann. Occup. Hyg. 38(Suppl 1):745-751 (1994).

Lockey, J. E. Nonasbestos Fibrous Minerals. Clin. Chest Med. 2(no. 2):203-218 (1981).

Lucas, J. The Cutaneous and Ocular Effects Resulting From Worker Exposure to Fibrous Glass. Occupational Exposure to Fibrous Glass. Proceedings of a Symposium. June 26-27, 1974. College Park, MD. HEW Pub. No. (NIOSH) 76-151. 1976. pp. 211-215 .

Luoto, K., Holopainen, M., and Savolainen, K. Scanning Electron Microscopic Study on the Changes in the Cell Surface Morphology of Rat Alveolar Macrophages After Their Exposure to Man-Made Vitreous Fibers. Environ. Res. 66(2):198-207 (1994).

Luoto, K., Holopainen, M., Sarataho, M., and Savolainen, K. Comparison of Cytotoxicity of Man-Made Vitreous Fibers. Ann. Occup. Hyg. 4(1):37-50 (1997).

Malmberg, P., Hedenstein, H. J., Kolmodin-Hedran, B., and Krantz, S. Pulmonary Function in Workers of a Mineral Rock Fibre Plant. Biological Effects of Man-Made Mineral Fibres. Proceedings of a WHO/IARC Conference, vol. 1. April 20-22, 1982. Copenhagen, Denmark. 1984. pp. 427-435.

Maltoni, C. and Minardi, F. Recent Results of Carcinogenicity Bioassays of Fibres and Other Particulate Matter. In: Non-Occupational Exposure to Mineral Fibres, edited by J. Bignon, J. Peto, and R. Saracci. IARC Scientific Pub. No. 90. Lyon: IARC. 1989. pp. 46-53.

Manke, J., Rödelsperger, K., and Woitowitz, H-J. Electron Microscope Identification of Mineral Fibers in Human Lung Tissue. Naturwissenschaften. 77(9):433-435. 1990.

Manville [Corporation]. Health and Safety Aspects of Refractory Ceramic Fibers. Report HSE-66B. 1990. 28p.

Manville. Two Year Inhalation Bioassay of Refractory Ceramic Fiber (RCF) in the Rat. 8EHQ-0691-0553 Suppl. February 18, 1991. Office of Toxic Substances, U.S. EPA, Washington, DC. 1991a.

Manville. Intratracheal Study of Four Different Ceramic Fibers in Fischer 344 Rats. 8EHQ-0691-0553 Suppl. June 10, 1991. Office of Toxic Substances, U.S. EPA, Washington, DC. 1991b.

Manville. Johns Manville Material Product MSDS. Available through Johns Manville Home Page @www.jm.com. Accessed 5 August 1997.

Maples, K. R. and Johnson, N. F. Fiber-Induced Hydroxyl Radical Formation: Correlation with Mesothelioma Induction in Rats and Humans. Carcinogenesis. 13(11):2035-2039 (1992).

Marconi, A., Corradetti, E., and Mannozzi, A. Concentration of Man-Made Vitreous Fibres During Installation of Insulation Material Aboard Ships at Ancona Naval Dockyards. Ann. Occup. Hyg. 31 (no. 4B):595-599 (1987).

Marsh, G. M., Enterline, P. E., Stone, R. A., and Henderson, V. L. Mortality Among a Cohort of US Man-Made Mineral Fiber Workers: 1985 Follow-up. J. Occup. Med. 32(7):594-604 (1990).

Mast, R. W., McConnell, E. E., Glass, L. R., Hesterberg, T. H., Thevenaz, P., Chevalier, J., and Anderson, R. A. Multiple Dose Chronic Inhalation Toxicity Study of Kaolin Refractory Ceramic Fiber (RCF) in Male Fischer 344 Rats. Toxicologist. 13:43 (1993).

Mast, R. W., McConnell, E. E., Anderson, R., Chevalier, J., Kotin, P., Bernstein, D. M., Thevenaz, P., Glass, L. R., Miiller, W. C., and Hesterberg, T. W. Studies on the Chronic Toxicity (Inhalation) of Four Types of Refractory Ceramic Fiber in Male Fischer 344 Rats. Inhal. Toxicol. 7:425-467 (1995a).

Mast, R. W., McConnell, E. E., Hesterberg, T. W., Chevalier, J., Kotin, P., Thevenaz, P., Bernstein, D. M., Glass, L. R., Miiller, W. C. and Anderson, R. Multiple-Dose Chronic Inhalation Toxicity Study of Size-Separated Kaolin Refractory Ceramic Fiber in Male Fischer 344 Rats. Inhal. Toxicol. 7:469-502 (1995b).

McClellan, R. O. Assessing Health Risks of Synthetic Vitreous Fibers: An Integrative Approach. Regul. Toxicol. Pharmacol. 20:S121-S134 (1994).

McClellan, R. O. and Hesterberg, T. W. Role of Biopersistence in the Pathogenicity of Man-Made Fibers and Methods for Evaluating Biopersistence: A Summary of Two Round-Table Discussions. Environ. Health Perspect. 102(Suppl. 5):277-283 (1994).

McClellan, R. O., Miller, F. J., Hesterberg, T. W., Warheit, D. B., Bunn, W. B., Kane, A. B., Lippmann, M., Mast, R. W., McConnell, E. E., and Reinhardt, C. F. Approaches to Evaluating the Toxicity and Carcinogenicity of Man-Made Fibers: Summary of a Workshop held November 11-13, 1991, Durham, North Carolina. Regul. Toxicol. Pharmacol. 16(3):321-364 (1992).

McConnell, E. E. Synthetic Vitreous Fibers - Inhalation Studies. Regul. Toxicol. Pharmacol. 20:S22-S34 (1994).

McConnell, E. E., Wagner, J. C., Skidmore, J. W., and Moore, J. A. A Comparative Study of the Fibrogenic and Carcinogenic Effects of UICC Canadian Chrysotile B Asbestos and Glass Microfibre (JM100). Biological Effects of Man-Made Mineral Fibres. Proceedings of a WHO/IARC Conference, vol. 2. April 20-22, 1982. Copenhagen, Denmark. 1984. pp. 234-250.

McConnell, E. E., Kamstrup, O., Musselman, R., Hesterberg, T. W., Chevalier, J.,Miiller, W. C., and Thevenaz, P. Chronic Inhalation Study of Size-Separated Rock and Slag Wool Insulation Fibers in Fischer 344/N Rats. Inhal. Toxicol. 6:571-614 (1994).

McConnell, E. E., Mast, R. W., Hesterberg, T. W., Chevalier, J., Kotin, P., Bernstein, D. M., Thevenaz, P., Glass, L. R., and Anderson, R. Chronic Inhalation Toxicity of a Kaolin-Based Refractory Ceramic Fiber in Syrian Golden Hamsters. Inhal. Toxicol. 7:503-532 (1995).

McDonald, J. C., Case, B. W., Enterline, P. E., Henderson, V., McDonald, A. D., Plourde, M., and Sebastien, P. Lung Dust Analysis in the Assessment of Past Exposure of Man-Made Mineral Fibre Workers. Ann. Occup. Hyg. 34(5):427-441 (1990).

Mettes, D. G. Glass fibers. In: Handbook of Fiberglass and Advanced Plastic Composites, edited by G. Lubin. New York: Robert E. Kreiger Publishing Company. 1975. pp. 143-181.

Miettinen, O. S. and Rossiter, C. E. Man-Made Mineral Fibers and Lung Cancer: Epidemiological Evidence Regarding the Causal Hypothesis. Scan. J. Work Environ. Health. 16:221-231 (1990).

Mitchell, R. I., Donofrio, D. J., and Moorman, W. J. Chronic Inhalation Toxicity of Fibrous Glass in Rats and Monkeys. J. Am. Coll. Toxicol. 5:545-575 (1986).

Monchaux, G., Bignon, J., Jaurand, M. C., Lafuma, J., Sebastien, P., Masse, R., Hirsch, A., and Goni, J. Mesothelioma in Rats Following Inoculation with Acid-Leached Chrysotile Asbestos and Other Mineral Fibers. Carcinogenesis. 2(3):229-236 (1981).

Moorman, W. J., Mitchell, R. T., Mosberg, A. T., and Donofrio, D. J. Chronic Inhalation Toxicology of Fibrous Glass in Rats and Monkeys. Ann. Occup. Hyg. 32(Suppl. 1):757-767 (1988).

Morgan, A. Effect of Length on the Clearance of Fibres From the Lung and on Body Formation. Biological Effects of Mineral Fibres. Proceedings of a Symposium, vol. 1, edited by J. C. Wagner. September 25-27, 1979. Lyon, France. IARC Scientific Pub. No. 30. 1980. pp. 329-335.

Morgan, A. and Davis, J. A. Effect of Chemical Composition on the Solubility of Glass Fibres *in vivo* and *in vitro*. Ann. Occup. Hyg. 38(Suppl. 1):609-617 (1994).

Morgan, A. and Holmes, A. The Deposition of Man-Made Mineral Fibers in the Respiratory Tract of the Rat, Their Subsequent Clearance, Solubility *in vivo* and Protein Coating. Biological Effects of Man-Made Mineral Fibres. Proceedings of a WHO/IARC Conference, vol. 2. April 20-22, 1982. Copenhagen, Denmark. 1984. pp. 1-17.

Morgan, A., Black, A., Evans, N., Holmes, A., and Pritchard, J. N. Deposition of Sized Glass Fibres in the Respiratory Tract of the Rat. Ann. Occup. Hyg. 23:353-366 (1980).

Morgan, A., Holmes, A., and Davison, W. Clearance of Sized Glass Fibers from the Rat Lung and Their Solubility *in vivo*. Ann. Occup. Hyg. 25:317-331 (1982).

Morgan, R. W., Kaplan, S. D., and Bratsberg, J. A. Mortality Study of Fibrous Glass Production Workers. Arch. Environ. Health. 36(4):179-183 (1981).

Mossman, B. T. and Sesko, A. M. *In vitro* Assays to Predict the Pathogenicity of Mineral Fibers. Toxicology. 60(issue 1-2):53-61 (1990).

Moulin, J. J., Mur, J. M., Wild, P., Perreaux, J. P., and Pham, Q. T. Oral Cavity and Laryngeal Cancers Among Man-Made Mineral Fibre Production Workers. Scan. J. Work Environ. Health. 12:27-31 (1986).

Muhle, H., Pott, F., Bellman, B., Takenaka, S., and Ziem, U. Inhalation and Injection Experiments in Rats to Test the Carcinogenicity of MMMF. Ann. Occup. Hyg. 31(no. 4B):755-764 (1987).

Muhle, H., Bellman, B., and Pott, F. Durability of Various Mineral Fibres in Rat Lungs. Proceedings of a NATO Advanced Research Workshop on Mechanisms in Fibre Carcinogenesis, vol. 223 (NATO ASI

Series), edited by R. C. Brown, J. A. Hoskins, and N. F. Johnson. October 22-25, 1990. Albuquerque, NM. 1991. pp. 181-187.

Musselman, R. P., Miiller, W. C., Eastes, W., Hadley, J. G., Kamstrup, O., Thevenaz, P., and Hesterberg, T. Biopersistence of Man-Made Vitreous Fibers (MMVF) and Crocidolite Fibers in Rat Lungs Following Short-Term Exposures. Environ. Health Perspect. 102(Suppl. 5):139-143 (1994).

Nambu, Z., Tanaka, I., and Kido. M. Effects of Glass Fiber Exposure on Rat Lungs. Jpn. J. Ind. Health. 34(2):140-141 (1992).

Nasr, A. N. M., Ditchek, T., and Scholtens, P. A. The Prevalence of Radiographic Abnormalities in the Chests of Fiber Glass Workers. J. Occup. Med. 13(8):371-376 (1971).

NAVMEDCOM (Naval Medical Command). Identification and Counting of Fibers in Thermal Insulation Materials. Letter to COMNAVSEASYSCOM (SEA 07C). March 17, 1986. 6271 Ser 242/0188.

NAVMEDCOM. Review of Draft COMNAVSEASYSCOM Thermal Insulation Control Program. Letter to COMNAVSEASYSCOM (OPR-07AE). April 30, 1987. 5100 Ser 242/0168.

NAVSEASYSCOM (Naval Sea Systems Command). Ceramic Fiber Insulation Material - Hazard Alert. Message 270051Z of August 27, 1985.

NAVSEASYSCOM. Ceramic Fiber Insulation Material - Classification of Hazard Alert. Message 291957Z of January 29, 1986a.

NAVSEASYSCOM. Modification of Mineral (Slag or Rock) Wool Exposure Limit. Message 312004Z of July 31, 1986b.

NAVSEASYSCOM. Thermal, Fire and Acoustic Insulation. Naval Ships' Technical Manual S9086-VH-STM-010, Chapter 635, 2nd Revision. 1990. 178 p.

NAVSEASYSCOM. Thermal, Fire and Acoustic Insulation. Naval Ships' Technical Manual S9086-VH-STM-010, Chapter 635, First Revision. 1986, with Advanced Change Notice (ACN) 1/A, March 1995. [Accessed on NSTM CD #N4667800015 0901-LP-012-1850. NSTM011, July 1997]

NIOSH (National Institute for Occupational Safety and Health). NIOSH Criteria for a Recommended Standard - Occupational Exposure to Fibrous Glass. DHEW (NIOSH) Pub. No. 77-152. Washington, DC: Government Printing Office. 1977a. 189 p.

NIOSH. NIOSH Manual of Analytical Methods, 2nd ed., vol. 1. P & CAM 239. HEW (NIOSH) Pub. No. 77-157. Cincinnati, OH: U.S. Department of Health and Human Services. 1977b.

NIOSH. Industrial Hygiene Surveys of Occupational Exposure to Mineral Wool. DHHS (NIOSH) Pub. No. 80-135. Cincinnati, OH: U.S. Department of Health and Human Services. 1980.

NIOSH. NIOSH Manual of Analytical Methods, 4th ed. DHHS (NIOSH) Pub. No. 94-113. Cincinnati, OH: U.S. Department of Health and Human Services. 1994.

NTP. Glasswool (Respirable Size). In: Seventh Annual Report on Carcinogens. 1994 Summary. U.S. Department of Health and Human Services, Public Health Service. 1994. pp.219-222.

Oberdorster, G. and Lehnert, B. E.: Toxicological Aspects of the Pathogenesis of Fiber-Induced Pulmonary Aspects. In: Mechanisms in Fiber Carcinogenesis, edited by R. C. Brown, J. A. Hoskins and N. F. Johnson. New York: Plenum Press. 1991.

OSHA (Occupational Safety and Health Administration). OSHA Industrial Hygiene Technical Manual. ISBN 0-86-587-205-8. Washington, DC:U.S. Department of Labor. 1984.

OSHA. Air Contaminants Proposed Rule. Federal Register 57:114, Book 2 of 2 Books, 12 Jun 1992a. p. 26002-26204.

OSHA. Air Contaminants. Federal Register 57:160, 18 Aug 1992b. p. 37126-37127.

OSHA. Code of Federal Regulations, Title 29, Part 1910, Section 1000. 1997.

Oshimura, M., Hesterberg, T. W., Tsutsui, T., and Barrett, J. C. Correlation of Asbestos-Induced Cytogenetic Effects with Cell Transformation of Syrian Hamster Embryo Cells in Culture. Cancer Res. 44:5017-5022 (1984).

Ottery, J., Cherrie, J., Dodgson, J., and Harrison, G. E. A Summary Report on the Environmental Conditions at 13 European Man-Made Mineral Fibre Plants. Biological Effects of Man-Made Mineral Fibres. Proceedings of a WHO/IARC Conference, vol. 1. April 20-22, 1982. Copenhagen, Denmark. 1984. pp. 83-117.

Owens-Corning. MSDS for Gold Calcium Silicate Pipe Insulation, MSDS No. 15-MSD-13619-F. Owens-Corning Fiberglas Corporation, Toledo, OH. 29 January 1994. 11p.

Perrault, G., Dion, C., and Cloutier, Y. Sampling and Analysis of Mineral Fibers on Construction Sites. Appl. Occup. Environ. Hyg. 7(5):323-326 (1992).

Phanprasit, W., Rose, V. E., and Oestenstad, R. K. Comparison of the Fibrous Aerosol Monitor and the Optical Fiber Count Technique for Asbestos Measurement. Appl. Ind. Hyg. 3(1):28-33 (1988).

Pickrell, J. A., Hill, J. O., Carpenter, R. L., Hahn., F. F., and Rebar, A. H. *In vitro* and *in vivo* Response After Exposure to Man-Made Mineral and Asbestos Insulation Fibers. Am. Ind. Hyg. Assoc. J. 44:557-561 (1983).

Pigott, G. H. A Classification System for Non-Asbestiform Fibres. Proceedings of a NATO Advanced Research Workshop on Mechanisms in Fibre Carcinogenesis, vol. 223 (NATO ASI Series), edited by R. C. Brown, J. A. Hoskins, and N. F. Johnson. October 22-25, 1990. Albuquerque, NM. 1991. pp. 539-545.

Pigott, G. H. and Ishmael, J. A Strategy for the Design and Evaluation of a "Safe" Inorganic Fiber. Ann. Occup. Hyg. 26:371-380 (1982).

Pigott, G. H., Gaskell, B. A., and Ishmael, J. Effects of Long Term Inhalation of Alumina Fibers in Rats. Br. J. Exp. Pathol. 62:323-331 (1981).

Possick, P. A., Gellin, G. A., and Key, M. M. Fibrous Glass Dermatitis. Am. Ind. Hyg. Assoc. J. 31:12-15 (1970).

Pott, F., Friedrichs, K. H., and Huth, F. Results of Animal Experiments on the Carcinogenic Effect of Fibrous Dusts and Their Interpretation with Regard to Carcinogenesis in Humans (German). Zbl. Bakt. Hyg. 162:467-505 (1976). [Cited in IARC, 1988]

Pott, F., Ziem, U., and Mohr, U. Lung Carcinomas and Mesotheliomas Following Intratracheal Instillation of Glass Fibres and Asbestos. Proceedings of the VIth International Pneumoconiosis Conference, vol. 2. September 20-23, 1983. Bochum, Federal Republic of Germany. 1984a. pp. 746-756.

Pott, F., Schlipköter, H. W., Ziem, U., Spurny, K., and Huth, F. New Results from Implantation Experiments with Mineral Fibres. Biological Effects of Man-Made Mineral Fibres. Proceedings of a WHO/IARC Conference, vol. 2. April 20-22, 1982. Copenhagen, Denmark. 1984b. pp. 286-302.

Pott, F., Ziem, U., Reiffer, F. J., Huth, F., Ernst, H., and Mohr, U. Carcinogenicity Studies on Fibres, Metal Compounds, and Some Other Dusts in Rats. Exp. Pathol. 32:129-152 (1987).

Pott, F., Roller, M., Ziem, U., Reiffer, F. J., Bellmann, B., Rosenbruch, M., and Huth, F. Carcinogenicity Studies on Natural and Man-Made Mineral Fibres with the Intraperitoneal Test in Rats. In: Non-Occupational Exposure to Mineral Fibres, edited by J. Bignon, J. Peto, and R. Saracci. IARC Scientific Pub. No. 90. Lyon: IARC. 1989. pp. 173-179.

Pott, F., Schlipköter, H. W., Roller, M., Rippe, R. M., Germann, P. G., Mohr, U., and Bellman, B. Carcinogenicity of Glass Fibres with Different Durability. Zbl. Hyg. 189:563-566 (1990). [Cited in Pott *et. al.*, 1991]

Pott, F., Roller, M., Rippe, R. M., Germann, P. G., and Bellman, B. Tumours by the Intraperitoneal and Intrapleural Routes and Their Significance for the Classification of Mineral Fibres. Proceedings of a NATO Advanced Research Workshop on Mechanisms in Fibre Carcinogenesis, vol. 223 (NATO ASI Series), edited by R. C. Brown, J. A. Hoskins, and N. F. Johnson. October 22-25, 1990. Albuquerque, NM. 1991. pp. 547-565.

Renne, R. A., Eldridge, S. R., Lewis, T. R., and Stevens, D. L. Fibrogenic Potential of Intratracheally Instilled Quartz, Ferric Oxide, Fibrous Glass, and Hydrated Alumina in Hamsters. Toxicol. Pathol. 13(4):306-314 (1985).

Rindel, A., Hugod, C., Bach, E., and Breum, N. O. Effect on Health of Man-Made Mineral Fibres in Kindergarten Ceilings. In: Non-Occupational Exposure to Mineral Fibres, edited by J. Bignon, J. Peto, and R. Saracci. IARC Scientific Pub. No. 90. Lyon: IARC. 1989. pp. 449-453.

Robinson, C. F., Dement, J. M., Ness, G. O., and Waxweiler, R. J. Mortality Patterns of Rock and Slag Mineral Wool Production Workers: An Epidemiological and Environmental Study. Br. J. Ind. Med. 39:45-53 (1982).

Roggli, V. L. Scanning Electron Microscopic Analysis of Mineral Fiber Content of Lung Tissue in the Evaluation of Diffuse Pulmonary Fibrosis. Scan. Microsc. 5(1):71-83. 1991.

Rood, A. P. and Streeter, R. R. Size Distributions of Airborne Superfine Man-Made Mineral Fibers Determined by Transmission Electron Microscopy. Am. Ind. Hyg. Assoc. J. 46(5):257-261 (1985).

RTECS® (Registry of Toxic Effects of Chemical Substances). On-Line Database, Available through National Library of Medicine. Produced by the National Institute for Occupational Safety and Health. Accessed 21 July 1997.

Rutten, A. A. J. J. L., Bermudez, E., Mangum, J. B., Wong, B. A., Moss, O. R., and Everitt, J. I. Mesothelioma Cell Proliferation Induced by Intrapleural Instillation of Man-Made Fibers in Rats and Hamsters. Fundam. Appl. Toxicol. 23(1):107-116 (1994).

Saracci, R., Simonato, L., Acheson, E. D., Andersen, A., Bertazzi, P. A., Claude, J., Charnay, N., Esteve, J., Frentzel-Beyme, R. R., Gardner, M. J., Jensen, O. M., Massing, R., Olsen, J. H., Teppo, L., Westerholm, P., and Zocchetti, C. Mortality and Incidence of Cancer Among Workers in the Man-Made Vitreous Fiber Producing Industry: An International Investigation in 13 European Plants. Br. J. Ind. Med. 41:425-436 (1984).

Schneider, R. Exposures to Man-Made Mineral Fibres in User Industries in Scandinavia. Ann. Occup. Hyg. 22:153-162 (1979).

Schneider, T. and Smith, E. D. Characteristics of Dust Clouds Generated From Old MMMF Products. Part II: Experimental Approach. Biological Effects of Man-Made Mineral Fibres. Proceedings of a WHO/IARC Conference, vol. 1. April 20-22, 1982. Copenhagen, Denmark. 1984. pp. 31-43.

Scholze, H. and Conradt, R. An *in vitro* Study of the Chemical Durability of Siliceous Fibres. Ann. Occup. Hyg. 31(no. 4B):683-692 (1987).

Shannon, H. S., Jamieson, E., Julian, J. A., Muir, D. C. F., and Walsh, C. Mortality Experience of Ontario Glass Fiber Workers - Extended Follow-up. Ann. Occup. Hyg. 31(no. 4B):657-662 (1987).

Shannon, H. S., Jamieson, E., Julian, J. A., and Muir, D. C. F. Mortality of Glass Filament (Textile) Workers. Br. J. Ind. Med. 47:533-536 (1990).

Simonato, L., Fletcher, A. C., Cherrie, J., Andersen, A., Bertazzi, P. A., Charnay, N., Claude, J., Dodgson, J., Estève, J., Frentzel-Beyme, R., Gardner, M. J., Jensen, O. M., Olsen, J. H., Saracci, R., Teppo, L., Winkelmann, R., Westerholm, P., Winter, P. D., and Zocchetti, C. The Manmade Mineral Fiber European Historical Cohort Study, Extension of the Follow-up. Scan. J. Work Environ. Health. 12:34-47 (1986).

Simonato, L., Fletcher, A. C., Cherrie, J., Andersen, A., Bertazzi, P. A., Charnay, N., Claude, J., Dodgson, J., Estève, J., Frentzel-Beyme, R., Gardner, M. J., Jensen, O. M., Olsen, J. H., Teppo, L., Winkelmann, R., Westerholm, P., Winter, P. D., Zocchetti, C., and Saracci, R. The International Agency for Research on Cancer Historical Cohort Study of MMMF Production Workers in Seven European Countries: Extension of the Follow-up. Ann. Occup. Hyg. 31:603-623 (1987).

Sincock, A. M., Delhanty, J. D. A., and Casey, G. A Comparison of the Cytogenic Response to Asbestos and Glass Fibre in Chinese Hamster and Human Cell Lines. Demonstration of Growth Inhibition of Primary Human Fibroblasts. Mutat. Res. 101:257-268 (1982).

Smith, D. M., Ortiz, L. W., Archuleta, R. F., and Johnson, N. F. Long-Term Health Effects in Hamsters and Rats Exposed Chronically to Man-Made Vitreous Fibres. Ann. Occup. Hyg. 31(no. 4B):731-754 (1987).

Smith, W. E., Hubert, D. D., Sobel, H. J., Peters, E. T., and Doerfler, T. E. Health of Experimental Animals Drinking Water With and Without Amosite Asbestos and Other Mineral Particles. J. Environ. Pathol. Toxicol. 3:277-300 (1980).

Spurny, K. R., Pott, F., Stöber, W., Opiela, H., Schörmann, J., and Weiss, G. On the Chemical Changes of Asbestos Fibers and MMMFs in Biologic Residence and in the Environment. Part 1. Am. Ind. Hyg. Assoc. J. 44(11):833-845 (1983).

Stanton, M. F. Some Etiological Considerations of Fibre Carcinogenesis. In: Biological Effects of Asbestos, edited by P. Bogovski, J. C. Gilson, V. Timbrell, and J. C. Wagner. Lyon: IARC. 1973. pp. 289-294.

Stanton, M. F. and Wrench, C. Mechanisms of Mesothelioma Induction with Asbestos and Fibrous Glass. J. Natl. Cancer Inst. 48(3):797-821 (1972).

Stanton, M. F., Layard, M., Tegeris, A., Miller, E., May, M., and Kent, E. Carcinogenicity of Fibrous Glass: Pleural Response in the Rat in Relation to Fiber Dimension. J. Natl. Cancer Inst. 58(3):587-603 (1977).

Stanton, M. F., Layard, M., Tegeris, A., Miller, E., May, M., Morgan, E., and Smith, A. Relation of Particle Dimension to Carcinogenicity in Amphibole Asbestos and Other Fibrous Minerals. J. Natl. Cancer Inst. 67:965-975 (1981).

Stokholm, J., Norn, M., and Schneider, T. Ophthalmologic Effects of Man-Made Mineral Fibers. Scan. J. Work Environ. Health. 8:185-190 (1982).

Sulzberger, M. B., Baer, R. L., Lowenberg, C., and Menzel, H. The Effects of Fiberglass on Animal and Human Skin - Experimental Investigation. Ind. Med 11:482-484 (1942). [Cited in NIOSH, 1977a]

Tilkes, F. and Beck, E. G. Comparison of Length-Dependent Cytotoxicity of Inhalable Asbestos and Man-Made Mineral Fibres. Biological Effects of Mineral Fibres. Proceedings of a Symposium, vol. 1, edited by J. C. Wagner. September 25-27, 1979. Lyon, France. IARC Scientific Pub. No. 30. 1980. pp. 475-483.

Tilkes, F. and Beck, E. G. Macrophage Functions After Exposure to Mineral Fibres. Environ. Health Perspect. 51:67-72 (1983).

TIMA (Thermal Insulation Manufacturers Association). Health and Safety Aspects of Man-Made Vitreous Fibers. Information, Data, Comments and Recommendations Regarding Occupational Exposure to Man-Made Vitreous Fibers. Submitted by TIMA, Inc. in Response to NIOSH Request for Comments and Secondary Data Relevant to Occupational Exposure to Synthetic and Natural Mineral Fibers, 55 Fed. Reg. 5073 (February 13, 1990). 1990. 347p.

Timbrell, V. The Inhalation of Fibrous Dusts. Ann. N Y Acad. Sci. 132:255-273 (1965).

Timbrell, V. Deposition and Retention of Fibres in the Human Lung. In: Inhaled Particles V, edited by W. H. Walton. Oxford: Pergamon Press. 1982. pp. 347-369.

Trethowan, W. N., Burge, P. S., Rossiter, C. E., Harrington, J. M., and Calvert, I. A. Study of the Respiratory Health of Employees in Seven European Plants that Manufacture Ceramic Fibres. Occup. Environ. Med. 52(2):97-104 (1995).

Utidjian, H. M. D. and deTreville, R. T. P. Fibrous Glass Manufacturing and Health: Report of an Epidemiological Study. Parts I and II. Proceedings of the 35th Annual Meeting of the Industrial Health Foundation. October 13-14, 1970. Pittsburgh, PA. IHF Bulletin No. 44. 1970. pp. 98-102.

van den Bergen, E. A., Rocchi, P. S. J., and Boogaard, P. J. Ceramic Fibers and Other Respiratory Hazards During the Renewal of the Refractory Lining in a Large Industrial Furnace. Appl. Occup. Environ. Hyg. 9(1):32-35 (1994).

Vu, V. T. Health Hazard Assessment of Nonasbestos Fibers. US EPA. Health and Environmental Review Division, Office of Toxic Substances. 1988. 251 p.

Vu, V. T. Assessment of the Potential Health Effects of Natural and Man-Made Fibers and Their Testing Needs: Prospectives of the U.S. Environmental Protection Agency. In: ILSI Monographs, edited by U. Mohr, D. L. Dungworth, J. L. Mauderly, and G. Oberdörster. Washington: ILSI Press. 1994. pp. 367-384.

Vu, V. T. and Dearfield, K. L. Biological Aspects of Fibrous Materials in Experimental Studies and Related Regulatory Aspects. In: Contemporary Issues in Fiber Toxicology, edited by D. B. Warheit. New York: Academy Press. 1993.

Wagner, J. C., Berry, G., and Timbrell, V. Mesotheliomata in Rats After Inoculation with Asbestos and Other Minerals. Br. J. Cancer. 28:173-185 (1973).

Wagner, J. C., Berry, G., and Skidmore, J. W. Studies on the Carcinogenic Effects of Fiber Glass of Different Diameters Following Intrapleural Inoculation in Experimental Animals. Occupational Exposure to Fibrous Glass. Proceedings of a Symposium. June 26-27, 1974. College Park, MD. HEW Pub. No. (NIOSH) 76-151. 1976. pp. 193-204.

Wagner, J. C., Berry, G. B., Hill, R. J., Munday, D. E., and Skidmore, J. W. Animal Experiments with MMM(V) Fibres - Effects of Inhalation and Intrapleural Inoculation in Rats. Biological Effects of Man-Made Mineral Fibres. Proceedings of a WHO/IARC Conference, vol. 2. April 20-22, 1982. Copenhagen, Denmark. 1984. pp. 209-234.

Warheit, D. B., Hwang, H. C., and Achinko, L. Assessments of Lung Digestion Methods for Recovery of Fibers. Environ. Res. 54(2):183-193 (1991).

Weill, H., Hughes, J. M., Hammad, Y. Y., Glindmeyer, H. W., Sharon, G., and Jones, R. N. Respiratory Health in Workers Exposed to Man-Made Vitreous Fibers. Am. Rev. Respir. Dis. 128:104-112 (1983).

Wheeler, C. S. Exposure to Man-Made Mineral Fibers: A Summary of Current Animal Data. Toxicol. Ind. Health. 6(2):293-307 (1990).

Wheeler, C. S. and Garner, C. D. A Comparison of the Toxicity of Asbestos, Non-Asbestos Fibers, and Semi-Metallic Brake Residue in a Macrophage-like Cell Line. General Motors Research Laboratories. GMR-6322. 1988. [Cited in Wheeler, 1990]

WHO (World Health Organization). Reference Methods for Measuring Airborne Man-Made Mineral Fibres (MMMF). WHO/EURO MMMF Reference Scheme. Environmental Health Report 4. Copenhagen: World Health Organization, Regional Office for Europe. 1985. pp.16-35.

Wong, O., Foliart, D., and Trent, L. S. A Case-Control Study of Lung Cancer in a Cohort of Workers Potentially Exposed to Slag Wool Fibres. Br. J. Ind. Med. 48:818-824 (1991).

Wright, G. W. Airborne Fibrous Glass Particles. Chest Roentgenograms of Persons with Prolonged Exposure. Arch. Environ. Health. 16(2):175-181 (1968).

Wright, G. W. and Kuschner, M. The Influence of Varying Lengths of Glass and Asbestos Fibres on Tissue Response in Guinea Pigs. In: Inhaled Particles IV, edited by W. H. Walton. Oxford: Pergamon Press. 1977. pp. 455-477.

Yu, C. P., Zhang, L., Oberdörster, G., Mast, R. W., Glass, L. R., and Utell, M. J. Clearance of Refractory Ceramic Fibers (RCF) From the Rat Lung: Development of a Model. Environ. Res. 65(2):243-253 (1994).